



August 2009

NIEHS Spotlight



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Institute's much anticipated Clinical Research Unit (CRU). ...[read more](#)



Birnbaum Maintains High Profile as Environmental Health Spokesperson

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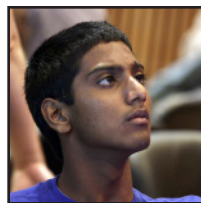


Speakers Present a Strategy for Sustainability

According to a team of public health scientists speaking at NIEHS on July 21, broad-based acceptance of sustainability as a guiding principle for

science, economics and society will require changes in attitudes about evaluation of risk from chemicals, an acceptance of scientific uncertainty, and what might seem to be unlikely partnerships.[read more](#)

Science Notebook



Program Kicks Off Active Learning Format for Summer Interns

NIEHS Summers of Discovery students got their first taste of the program's new emphasis on

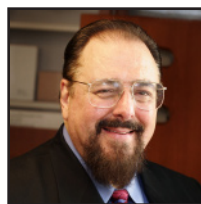
active learning during a July 1 seminar on DNA repair, presented by NIEHS Principal Investigator Thomas Kunkel, Ph.D.. ...[read more](#)



Public Comments Invited on Ocular Safety Testing Recommendations

The National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative

Toxicological Methods (NICEATM), in conjunction with the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM), announced the availability of an independent scientific peer review panel report on alternative ocular safety testing methods and approaches and invited public comments in the July 13 issue of the *Federal Register*. ...[read more](#)



Sun Exposure May Trigger Certain Autoimmune Diseases in Women

Ultraviolet (UV) radiation from sunlight may be associated with the development of certain

autoimmune diseases, particularly in women, according to a new study by researchers at the NIEHS.[read more](#)

NIEHS Spotlight



Meet Rachel Gross — A Stimulus Funding Success Story

During the past year, timing — good and bad — has played an important role in the life of Rachel Gross, newly

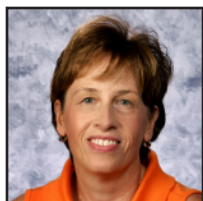
hired management analyst for the NIEHS Division of Extramural Research and Training (DERT) Office of the Director. ...[read more](#)



Robertson Promotes NIEHS at SLA Centennial

NIEHS Library Director Dav Robertson was in Washington June 14–17 in his role as chair of the Special Libraries Association

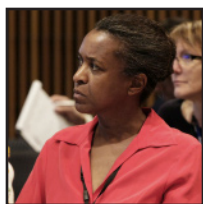
(SLA) Centennial Commission and 2009 Conference Committee, when the group celebrated its 100th anniversary at the annual meeting at the Walter E. Washington Convention Center. ...[read more](#)



Grant Named to Board of Bioscience Education Group

On July 1, NIEHS Deputy Chief of the Comparative Medicine Branch Mary Grant, V.M.D., began a three-year term as a member of the board of directors

of the North Carolina Association for Biomedical Research (NCABR).[read more](#)



NTP Leadership Looks Forward at Summer Board Meeting

When the National Toxicology Program (NTP) Board of Scientific Counselors (BSC) met at NIEHS July 23–24, the group faced the usual order of business

with reviews, reports, nominations and concepts, and interagency agreements. Early in the meeting, members also learned of new developments on the horizon in regard to public health and communication of potential health risk, as the NTP enters its fourth decade and evolves to meet the challenge of the NTP Vision for the 21st Century.[read more](#)

Science Notebook



NIEHS Investigators Explore Biochemical Causes of Mitochondrial Disease

A recent study published in the July 17 issue of the *Journal*

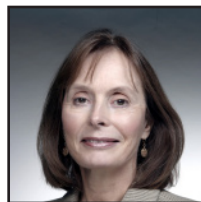
of *Biological Chemistry* explored how certain DNA mutations may contribute to genesis and progression of mitochondrial diseases.[read more](#)



Mouse Model Shows Early Symptoms of Parkinson's Disease

In a new study funded in part by NIEHS and published in the June 24 issue of the *Journal of*

Neuroscience, Emory University scientists unveiled a new mouse model with reduced monoamine storage capacity that manifests the early non-motor symptoms of Parkinson's disease (PD). ...[read more](#)



Child's IQ Can Be Affected by Mother's Exposure to Urban Air Pollutants

A mother's exposure to urban air pollutants known as polycyclic aromatic hydrocarbons (PAHs)

can adversely affect a child's intelligence quotient or IQ, a new study in the journal *Pediatrics* reports. ...[read more](#)



New Treatment May Help with Side Effects of Chemotherapy

A new study funded in part by NIEHS reports experimental findings that may help prevent

a dangerous side effect of the widely used chemotherapeutic drug cisplatin. ...[read more](#)

NIEHS Spotlight



NIEHS Launches Intramural Awareness Campaign

As part of a three-month NIH-wide campaign to raise the visibility of the Intramural Program, investigators in the NIEHS Division of Intramural Research (DIR) staffed a table at the Institute's cafeteria and handed out nearly 75 promotional coffee mugs. ...[read more](#)



Superfund Holds Teacher Workshop on Water Quality

Hundreds of middle and high school students will be learning about the latest advances in water quality research and remediation this academic year, thanks to the NIEHS-funded University of North Carolina at Chapel Hill (UNC-CH) Superfund Research Program (SRP). ...[read more](#)



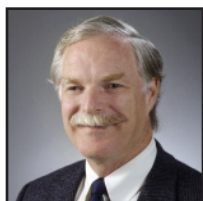
SOT Holds Reception for Birnbaum

The Society of Toxicology (SOT) honored its former president, NIEHS and National Toxicology Program (NTP) Director Linda Birnbaum, Ph.D., with a Capitol Hill reception on July 8 in Washington.[read more](#)



High School Researcher at Dartmouth Wins Award

Nick Sinnott-Armstrong, a high-school student who completed a summer research project in the Dartmouth College Superfund Research Program (SRP), took first prize for his work in a programming contest at the Genetic and Evolutionary Computation Conference (GECCO), held July 8–12 in Montreal. ...[read more](#)



Friends and Colleagues Mourn the Passing of K.C. Donnelly

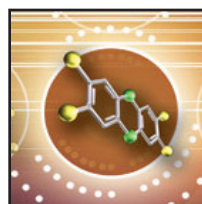
Following an extended battle with esophageal cancer, long-time Superfund Research Program (SRP) grantee K. C. Donnelly, Ph.D., died on July 1 in College Station, Texas at age 57. He is survived by his wife, Ruth, two sons and daughters-in-law, brother and sister.[read more](#)

Science Notebook



Combined Biomarkers Improve Accuracy of Prostate Cancer Detection

According to data from 2004–2006, the National Cancer Institute estimates that one in six American men will be diagnosed with prostate cancer during their lifetime. Since early detection of the disease increases the likelihood of survival, physicians routinely use serum prostate specific antigen (PSA) screening and subsequent tissue biopsy to determine whether a patient has prostate cancer. ...[read more](#)



This Month in EHP

The August issue of *Environmental Health Perspectives (EHP)* explores “The Future of Toxicity Testing” with a Focus article on the Tox21 partnership of the National Toxicology Program, the NIH Chemical Genomics Center and U.S. Environmental Protection Agency that seeks to transform toxicology testing for the 21st century. ...[read more](#)



David Sinclair to Present Distinguished Lecture August 11

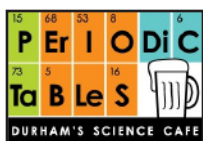
The 2008-2009 NIEHS Distinguished Lecture Series will conclude August 11 with a talk by Harvard University molecular geneticist David Sinclair, Ph.D. Sinclair's lecture on “Pathways That Control the Pace of Aging and Disease: Prospects for New Medicines” will begin at 11:00 a.m. in Rodbell Auditorium and be hosted by NIEHS Mammalian Aging Group Principal Investigator Xiaoling Li, Ph.D.. ...[read more](#)

Inside the Institute



Community Support Aids Green Science Camp

The Durham Alumnae Chapter of Delta Sigma Theta Sorority provided a fun-filled day for children and adults with a focus on green science at the fourth annual Science and Everyday Experiences (SEE) day camp on July 11. ...[read more](#)



Wilcox Wows the Crowd at Science Café

Speaking at the Broad Street Café in Durham, N.C. on July 14, NIEHS epidemiologist Allen Wilcox, M.D., Ph.D., gave an informal talk on human fertility to a capacity audience made up largely of non-scientists. The talk was one of the Science Café's "Periodic Tables" events organized by the Museum of Life and Science in Durham. ...[read more](#)

Calendar of Upcoming Events

- **August 4**, in Rodbell Auditorium, 8:00–6:00 — International Office Seminar
- **August 5**, in Rodbell Auditorium, 11:00–12:00 — Summers of Discovery Seminar Series on "Basic Concepts of Epidemiology" with Dale Sandler, Ph.D., and Allen Wilcox, M.D., Ph.D.
- **August 6**, in Rodbell Auditorium, 7:00–5:00 — Community Resources Festival
- **August 11**, in Rodbell Auditorium, 11:00–12:00 — Distinguished Lecture Seminar Series featuring David Sinclair, Ph.D., speaking on "Pathways that Control the Pace of Aging and Disease: Prospects for New Medicines"
- **August 12–14**, in Rodbell Auditorium, 8:00–5:00 — Obesity and the Built Environment Grantee Meeting
- **August 31**, in Rall F193, 1:00–2:30 — Seminar on "Properties of Yeast DNA Polymerase Epsilon — Implications for Leading Strand Synthesis" with Erik Johansson, Ph.D.
- **September 1**, in Rodbell Auditorium, 1:00–5:30 — NIEHS Genomics Day
- View More Events: [NIEHS Public Calendar](#)

Extramural Research

Extramural Update

Pursuant to its role under the Superfund Amendments and Reauthorization Act of 1986 (SARA), on July 9 the NIEHS Worker Education and Training Program issued Requests for Applications (RFAs) for two new funding opportunity announcements (FOAs)— Hazardous Materials Worker Health and Safety Training (RFA-ES-09-004) and Hazmat Training at Department of Energy (DOE) Nuclear Weapons Complex (RFA-ES-09-003). ...[read more](#)

Extramural Papers of the Month

- [HLA-DR4 – Possible Risk Gene for Autism](#)
- [Endocrine Society Position Statement on Endocrine Disruptors](#)
- [Bisphenol A Study Shows Reproductive Health Effects](#)
- [New Method May Accelerate Drug Discovery for Parkinson's](#)

Intramural Research

Intramural Papers of the Month

- [Multivitamin Intake Is Associated with Longer Telomeres](#)
- [Pesticides Are Associated With Allergic Asthma in Male Farmers](#)
- [A Missense Mutation in *repro32* Mutant Male Mice Causes Infertility](#)
- [Elucidation of the Cu,Zn-Superoxide Dismutase Peroxide Cycle](#)

NIEHS Spotlight

NIEHS Holds Ribbon Cutting for Clinical Research Unit

By Eddy Ball

Friends, supporters and dignitaries flocked to the NIEHS campus on July 27 in precedent-setting numbers to celebrate the grand opening of the Institute's much anticipated Clinical Research Unit (CRU).

The day's events began with addresses to a capacity audience in Rodbell Auditorium by distinguished visitors, before moving to the CRU where there was a formal ribbon cutting ceremony and refreshments. In the afternoon, visitors joined NIEHS scientists and employees for presentations on aspects of clinical research ([see text box](#)).

The morning talks, which were moderated by Emcee Joe Graedon, radio celebrity and co-host of the public radio program "[The People's Pharmacy](#)," opened with welcome remarks by NIEHS and National Toxicology Program Director Linda Birnbaum, Ph.D.

"Opening this unit has been a long time coming," Birnbaum said, "but I believe that it is something that will not only benefit our researchers, but our community and nation as well." She called the CRU a "clinical training ground" that will foster innovative collaborations.

Birnbaum was followed with "Greetings" from NIH Deputy Director for Intramural Research Michael Gottesman, M.D., and "A Local Partner's Perspective" by Robert Califf, M.D., vice chancellor for clinical research at Duke University.

Thanks to Graedon's vigilance, each of the politicians on hand kept remarks within the allotted three minutes. U.S. Senator Kay Hagan was lead speaker from the federal delegation, which included 4th District Congressman David Price, Ph.D., 2nd District Congressman Bob Etheridge and 13th District Congressman Brad Miller. Each expressed support for the environmental research and public health mission of NIEHS and NTP as well as for funding for health research at NIH.



Graedon drew upon his radio experience to make sure the talks stayed on time. He introduced his wife and "The People's Pharmacy" co-host, medical anthropologist Terry Graedon, Ph.D., who was in the audience. (Photo courtesy of Steve McCaw)



Birnbaum acknowledged the vision of former NIEHS Director David Schwartz, M.D., in recognizing the need for a clinical research facility at the Institute. "It puts the public health mission of our Institute front and center," she said of the CRU. (Photo courtesy of Steve McCaw)

As cameras flashed, politics became progressively more local in scope, starting with N.C. Lieutenant Governor Walter Dalton and N.C. Secretary of Health and Human Services Lanier Cansler. The state officials praised NIEHS and NTP for their contribution the state's growth in the area of biotechnology and for anticipating health issues in order to head off emerging problems.

Closing out the "Officials" portion of the program were Durham County Commissioner Michael Page and Durham Mayor William Bell, who thanked NIEHS for being the source for the many jobs his constituents fill at the Institute and for ensuring diversity among study participants.

NIEHS Acting Clinical Director Darryl Zeldin, M.D., concluded the formal portion of the celebration with the presentation of awards to 12 employees for their contributions to realizing the dream of clinical research at NIEHS, as well as thanks to many others who supported the CRU since its initial conception in 2005.

Under an unforgiving sun, visitors, many dressed to the nines, trekked to the other end of the main building and across the parking lot to the CRU. Following the ribbon cutting at the front door, they enjoyed a light buffet and the company of friends old and new — to say nothing of blessed sanctuary from the noontime heat and humidity.

After a lunch break, an equally enthusiastic audience returned to Robell Auditorium for talks about clinical research and public health translation hosted by NIEHS CRU Medical Director Stavros Garantziotis, M.D. Three distinguished physician scientists addressed their own work along the broad spectrum of what Birnbaum has called "bench-to-bedside and bench-to-public health" translational research — Robert Califf, M.D., vice chancellor for clinical research at Duke University; National Children's Study Principal Investigator Philip Landrigan, M.D., of Mt. Sinai Medical Center; and Franck Mauvais-Jarvis, M.D., Ph.D., a Northwestern University Division of Endocrinology, Metabolism and Molecular Medicine associate professor of medicine.



With scissors in hand, NIEHS leaders and guest speakers prepared to mark the grand opening of the CRU. Shown from left to right were Birnbaum, Gottesman, Cansler, Miller, Califf, Etheridge, Bell, Hagan, Price, Graedon, Dalton, Page and Zeldin. (Photo courtesy of Steve McCaw)



Senator Kay Hagan, left, and NIEHS Director Linda Birbaum posed together during the reception at the CRU. Hagan said it is "critical to fund" research at NIEHS. (Photo courtesy of Steve McCaw)

Clinical Research Symposium



Mayor Bell, left, talked with Congressman Price. Price praised the CRU as “an exciting part of the program of an institute on the move.” He said he foresees more “life-saving and life-enhancing research” as well from such leading-edge efforts as the Sister Study. (Photo courtesy of Steve McCaw)



NIEHS Acting Scientific Director John Pritchard, Ph.D., enjoyed a photo opportunity with Gottesman, who oversees the largest clinical research hospital in the U.S. Birnbaum gave special thanks to Gottesman for his support at the NIH level. (Photo courtesy of Steve McCaw)

- Back at the podium for a talk on “A Strategic Approach to Addressing the Needs for Mechanistic Clinical Research,” Robert Califf explored the leadership challenges of realizing the integrated, multi-disciplinary model that is at the heart of the NIH Clinical and Translational Science Awards program. Looking back on his own experience with medicines that delivered less than they promised — or even produced adverse effects in patients — Califf argued that a network of multi-disciplinary programs could help researchers understand more completely the true clinical outcomes that may be obscured by focusing too intently on surrogate endpoints in drug development. He also told the audience about Duke’s global initiatives in Singapore and New Delhi.
- Long-time NIEHS grantee Philip Landrigan spoke on the “The National Children’s (NCS) Study — The Need and the Promise.” Landrigan began his talk with a look back at the success of translating research on lead into a public health policy that has reduced blood levels in the population by some 90 percent in the past 30 years. He expressed his confidence that the growing network of NCS research sites, such as the one he leads in Queens, will use data from the long-term prospective study of 100,000 children to have similar effects in decades to come — translating the results of molecular epidemiology from the bench, the clinic and the desk to public health policy.
- The final speaker of the afternoon was Franck Mauvais-Jarvis, who recounted his clinical research in a talk on “Estrogen Receptors and Pancreatic Islet Survival in Diabetes: An Example of Bidirectional Translational Research.” Helped by his collaborations with NIEHS Principal Investigator Ken Korach, Ph.D., Mauvais-Jarvis explored an hypothesis born of clinical observation and tested in engineered mice that he anticipates within five years will help patients in clinical trials — just where his bidirectional bedside-to-bench/bench-to-beside odyssey originally began.



Landrigan referred to the legacy of former NIEHS Director David Rall, M.D., Ph.D., as he recalled meeting in the 1970s at NIEHS in the campaign to ban lead from gasoline. His Queens site was one of the first two counties to begin recruitment for the National Children's Study earlier this year. (Photo courtesy of Steve McCaw)



Garantziotis expressed his hope that the Clinical Research Symposium would be the first in a series of symposia on clinical research and translational medicine, as results from studies at the CRU begin to emerge. (Photo courtesy of Steve McCaw)



Califf, center, enjoys banter with his host prior to his talk. He described his experience with the intervention drugs encainide and flecainide that taught him to question the validity of surrogate endpoints in true clinical outcomes. "Most of the time what we thought would work, didn't," he noted. (Photo courtesy of Steve McCaw)



Mauvais-Jarvis' bedside observation that human pancreatic islet failure is much more common in men than in women with Type 1 diabetes took him back the bench for animal studies. He discovered that raising estrogen to physiologic levels could be protective — a strategy he hopes soon to test with humans. (Photo courtesy of Steve McCaw)

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Birnbaum Maintains High Profile as Environmental Health Spokesperson

By Eddy Ball

In the space of just over two weeks, NIEHS and National Toxicology Program (NTP) Director Linda Birnbaum, Ph.D., spread her message of renewal and challenge to hundreds more people nationwide, underscoring the urgency of promoting environmental public health and reducing adverse health effects of chemical exposures. Her audiences included scientists, regulators, public health specialists, industry representatives and members of the general public at venues in Washington, Durham, N.C., and Aspen, Colo.

On June 26 at the Ronald Reagan Building and International Trade Center, Birnbaum delivered a keynote address during the launch of the Centers for Disease Control and Prevention (CDC)-sponsored [National Conversation on Public Health and Chemical Exposures](#), speaking to some 400 attendees in Washington and more than 100 viewers of the event's webcast. Birnbaum joined U.S. Environmental Protection Agency Administrator Lisa Jackson as plenary speakers in a program moderated by Howard Frumkin, M.D., Dr.P.H., director of the CDC National Center for Environmental Health Agency for Toxic Substances and Disease Registry as the first step in outlining a concerted national agenda.

In an [interview](#) at the studio of WUNC public radio recorded for broadcast as 703 Health News Update on July 11–12, “People’s Pharmacy” hosts Joe Graedon and Terry Graedon, Ph.D., talked with Birnbaum about her vision for future directions in environmental health sciences research and public health. Birnbaum also used this opportunity to explain the work and importance of NTP to a general public audience.

At the Given Institute in Aspen on July 13, Birnbaum addressed attendees at the [35th Annual Summer Meeting of the Toxicology Forum](#). Her remarks there on the “New Vision for NIEHS and NTP” set the stage for a weeklong series of sessions and updates on issues in applied and regulatory toxicology with an appeal for public-private partnerships to pool resources in a united effort to better manage chemicals in the environment.

During each of her public appearances, Birnbaum challenged the status quo in environmental science and regulation as she delivered an appeal for concerted action by citizens, advocates and scientists to address environmental health threats on a local and global level. Birnbaum reviewed the successes of the past 40 years of environmental action and the research underway funded through NIEHS and NTP — ranging from basic research and epidemiology to specialized research centers throughout the country and hands-on worker training programs.

As in past talks, Birnbaum appealed to civic responsibility and spoke of the country’s new emphasis on environmental public health. “Health and the environment are increasingly a priority for the nation, and new issues are emerging,” she told her audiences. “We have it within our responsibility to help all of our people to live longer, more productive lives in better health and with better prospects.”



Birnbaum, shown at an earlier lecture at NIEHS, highlighted NTP and initiatives in global warming, nanotechnology and green chemistry in recent talks. (Photo courtesy of Steve McCaw)

Birnbaum also spoke of the need to marshal resources to realize the benefits of cooperative action and take toxicology into a new era of protecting people equitably from environmental hazards. She pointed to “new methodologies for efficient and thorough toxic assessments” that will help scientists better understand the affects of aggregate chemical exposures. She acknowledged the need to complement the “gold standard” cancer risk assessments developed over the three decades that the NTP has provided the American public with high-quality information “on such health effects as reproductive and developmental outcomes, neurological outcomes and immunological outcomes” from chemical exposures early in life.

Themes that ran through all of Birnbaum’s talks included making “the whole of NIEHS and NTP greater than the parts” by integrating the Institute’s research programs into a renewed mission. Echoing her earlier comments about the public health emphasis of NIEHS/NTP research, she emphasized that “prevention is the name of the game for us.”

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Speakers Present a Strategy for Sustainability

By Eddy Ball

According to a team of public health scientists speaking at NIEHS on July 21, broad-based acceptance of sustainability as a guiding principle for science, economics and society will require changes in attitudes about evaluation of risk from chemicals, an acceptance of scientific uncertainty, and what might seem to be unlikely partnerships. The three University of Massachusetts Lowell professors presented their arguments during a seminar on “Sustainable Production: A Path Toward Disease Prevention and Health Promotion” hosted by NIEHS and National Toxicology Program Director Linda Birnbaum, Ph.D.

The presenters are members of the trans-disciplinary [Lowell Center for Sustainable Production](#), which was established in 1995 to develop practical solutions to environmental and health problems — helping to advance changes that lead to a safer, more secure and sustainable planet. Speaking about the Center’s agenda and challenges were Project Director and Associate Professor of Community Health and Sustainability Joel Tickner, Sc.D.; Chair of the Department of Work Environment David Kriebel, Sc.D.; and [NIEHS grantee](#) and Chair of the Department of Community Health and Sustainability Craig Slatin, Sc.D.

In the course of their work, scholars at the Center have challenged the conventional scientific understanding of causality that they call “the reactionary principle.” They have taken science out of the lab to users of chemicals, developed a broad-based social, participatory process for engaging people about the potential dangers of chemical exposures, and they have assumed responsibility for coming up with answers and a wide range of viable alternatives for potentially hazardous chemicals.

Tickner opened the “tag-team” presentation with a discussion of the Center’s history and mission. “What we’ve tried to do,” he explained, “is bring together health and environment” by studying the problems and developing workable solutions and alternatives. An important part of the Center’s work, he said, is community involvement



In conventional risk assessment, Tickner observed, “We wait and we wait and we wait for a very high level of evidence, and in that time we’re not acting.” (Photo courtesy of Steve McCaw)

or “strategic engagement” of a broad range of sectors of society — including industry, companies that use chemicals, scientists who develop chemicals and plastics, and government, as well as labor and anti-poverty advocates. “We think it’s important to start with a high vision,” he noted, “but then work [proactively] within the pragmatic realities to realize solutions.”

In his part of the presentation, Kriebel elaborated on “the philosophical conundrum” that Tickner said plagues the process of assessing risk and determining causality in regard to chemicals. “Most people and most scientists,” Kriebel began, “have this mental model that there is some threshold of evidence that you need to get over” to establish a causal link between exposures and adverse health effects to justify action.

According to Kriebel, however, causality can be seen instead as a continuum, where much lower levels of evidence may justify a progression of interventions, beginning, for example, with eliminating unnecessary uses of chemicals and the use of alternatives. “How much evidence you need,” he argued, “depends on whether you have alternatives... to achieve the same social good without the hazards,” using a European-like “precautionary principle” and deciding what is a “plausibly safer” option.

Slatin closed out the team’s presentation with a focus on successes and hopeful signs, as well as bold new partnerships that would have appeared unlikely not long ago — such as blue-green alliances uniting labor, community, environmental and other groups in recent efforts. Because much of the problem with chemicals, public health and the environment is rooted in production, Slatin said, a comprehensive approach to sustainability needs to include a consideration of jobs that will be lost in the push for sustainability.

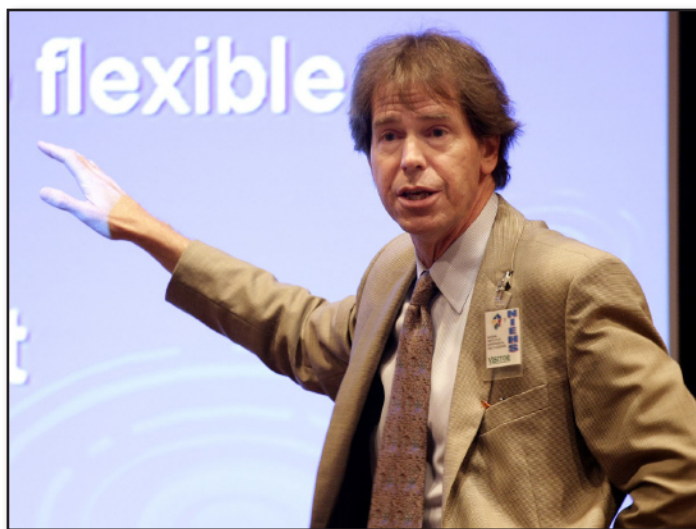
“Every time that we do something to manipulate our environment,” Slatin concluded, “there is something that is going to have a negative impact on us, as well as a positive impact.... Participation is fundamental, not secondary, in this process.”



Slatin, who is the author of a book on labor and the Superfund, focused on the need for broad-based alliances. “It has to be a democratic process [when economic change is involved],” he argued, “if you want it to be sustainable.” (Photo courtesy of Steve McCaw)



The presentation drew people from throughout the Institute, including NIEHS Molecular and Genetic Epidemiology Group Biologist Gleta Carswell, left, and Summers of Discovery Intern Sara Mishamandani. (Photo courtesy of Steve McCaw)



“What we’re trying to do is shift the focus of interest,” Kriebel explained, “away from ‘are we quantifying the risk correctly’ to ‘are there alternatives’ and ‘is there enough evidence to support a shift’” from a potentially harmful chemical to an alternative. (Photo courtesy of Steve McCaw)

Meet Rachel Gross — A Stimulus Funding Success Story

By Eddy Ball

During the past year, timing — good and bad — has played an important role in the life of Rachel Gross, newly hired management analyst for the NIEHS Division of Extramural Research and Training (DERT) Office of the Director. Gross is the first person hired at the Institute through the little known [NIH Administrative Fellows Program \(AFP\)](#) into a position funded through the [American Recovery and Reinvestment Act \(ARRA\)](#).

Gross graduated from North Carolina State University with a masters in public administration focusing on policy and environmental management in December 2008, only to launch her job search at the worst time in decades. She estimates she sent out five to ten resumes each week in the months that followed, resulting in sporadic interviews at best.

Along the way, Gross learned about fellowship opportunities at NIH and other agencies, and that was when her luck and timing began to change. In June, thanks to good timing and help from AFP and ARRA, Gross started her new job at NIEHS — a perfect example of the way ARRA is intended to promote job creation in what DERT Acting Director Gwen Collman, Ph.D., described as a “win-win for everyone.”

A resident of Raleigh for the past two years, Gross brings a varied background to her new job, united by, she says, her desire “to serve and empower people.” She started out with a bachelor’s degree in youth ministry and physical education from Toccoa Falls College in northeast Georgia, on a career path that led her to positions in youth programs and mental health services.

After her first job as a youth leader in her hometown of Savannah, Ga., Gross worked in Seattle before moving back east to North Carolina, where her family had moved and where she decided to pursue her interests in public health, policy and the environment. Last summer, she had her first taste of working in government as a program developer in water conservation for the Town of Cary.

Gross described landing her job at NIEHS, which until this spring she wasn’t aware even existed, as “serendipity” — it was the one place where location and vocation meshed ideally for her, and the timing turned out to be perfect. “As I understand it, the position here would not have existed if ARRA funding had not become available at just the right time,” she said.

Under the terms of her administrative fellowship, Gross will spend the next two years working closely with Collman and DERT Acting Deputy Director Pat Mastin, Ph.D., helping to coordinate the various activities related to ARRA. Gross will work with staff in all of the different branches within DERT and spend up to 90 days in rotations in other parts of the Institute and NIH.

“We’ll pair her up with other offices that also have ARRA activities,” Collman said, “such as the Financial Management Branch and Office of Science Policy.... We’re fortunate to have a very bright, motivated, highly capable individual to come and help us out.”



Gross, above, was interviewed initially in Bethesda and “was rated one of the best candidates they [AFP] had,” said NIEHS Administrative Officer Margarita Roque. “When ARRA came, it was the right time and the right place — and she hit the ground running.” (Photo courtesy of Steve McCaw)

As Collman explained, the two-year AFP position dovetails nicely with the ARRA timeframe. At the end of Gross' two year fellowship, she will be evaluated for a permanent position within DERT or elsewhere in the Institute. "At that point," Gross explained, "we should have figured out how my skills best meet the needs of NIEHS — not just in ARRA-related projects but in the Institute as a whole."

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Robertson Promotes NIEHS at SLA Centennial

By Eddy Ball

[NIEHS Library](#) Director Dav Robertson was in Washington June 14–17 in his role as chair of the Special Libraries Association (SLA) Centennial Commission and 2009 Conference Committee, when the group celebrated its 100th anniversary at the annual meeting at the Walter E. Washington Convention Center.

Robertson was recognized with a speaking role at the [SLA Centennial](#) opening session welcoming the 6,000 attendees. He was followed by the keynote speaker, former Secretary of State Colin Powell. On June 16, Robertson was part of the SLA Salutes! Award and Leadership Reception held in the Great Hall of the Library of Congress.

During the rest of the meeting, Robertson was on hand for professional development and networking, along with four others from NIEHS — Biomedical Librarians Larry Wright, Ph.D., and Stephanie Holmgren and Library Assistants Brendan Thompson and Katie Jelen, student interns from the University of North Carolina at Chapel Hill on their first trip to an SLA meeting.

"Our involvement in SLA is a good way of promoting NIEHS to the organization's 11,000 members worldwide," Robertson explained. "These specialized information professionals are the people who serve as conduits for getting information about NIEHS to their constituents — the people back at the university, the research institute or wherever special librarians are at work."

Robertson and his staff are active in the SLA Biomedical and Life Sciences Division, where specialized information professionals in the field share information about new technologies and methodologies in special sessions over the four-day conference. "This is really our primary resource for updating our skills and for networking," Robertson said. "We can bring leading-edge technology and strategies back to apply here at NIEHS to benefit our scientists."

At the division's business meeting and luncheon on June 16, *Nature* was honored as the most influential journal of the past century, and Robertson presented Elsevier with an award as the most influential publisher.



Powell, left, posed with Robertson following the keynote address. Under Powell's leadership, the Department of State invested heavily in the special resources of the Ralph Bunche Library, which was founded by Thomas Jefferson in 1789. (Photo courtesy of Mark Rinerston, The Photo Group)

The Centennial closed on June 17 with a general session on innovation in information featuring moderator Judy Woodruff of the Public Broadcasting Service (PBS) program “News Hour” with panelists [Neil deGrasse Tyson, Ph.D.](#), a Hayden Planetarium astrophysicist featured on the PBS program “NOVA,” *Forbes* Magazine Senior Editor Robyn Meredith and former IBM vice president of Internet technology John Patrick.

From the organization’s beginning, SLA members have taken pride in being pioneers in a new and ever-evolving kind of librarianship, one devoted to using practical information to achieve positive results in business, government, social agencies and parts of the academic community (see related February 2009 [story](#)).

The group’s Centennial is a yearlong celebration with events scheduled through the end of 2009. According to Robertson, attendance at this year’s conference was up 16 percent — at a time, he noted, when many organizations are experiencing a decline of as much as 30 percent.

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In the Great Hall of the Library of Congress, a bust of Jefferson, whose personal library made up the first volumes of the collection, overlooked SLA members at the banquet and reception. Special lighting added to the atmosphere as attendees mingled with a string quartet playing in the background. (Photo courtesy of Mark Rinerston, The Photo Group)

Grant Named to Board of Bioscience Education Group

By Eddy Ball

On July 1, NIEHS Deputy Chief of the Comparative Medicine Branch Mary Grant, V.M.D., began a three-year term as a member of the board of directors of the North Carolina Association for Biomedical Research (NCABR). She was one of four prominent members of the state’s bioscience research community elected at the board’s June 26 meeting.

Grant replaces her NIEHS colleague Diane Forsythe, D.V.M., chief of the Comparative Medicine Branch, as the board’s *ex officio* member.

“We’re delighted to have Mary as a new member of the [NCABR](#) board of directors, representing NIEHS,” said NCABR President Suzanne Wilkison. “She has played an integral role over the years at the NCABR ‘Rx for Science Literacy’ teacher professional development [programs](#) held annually at NIEHS.”

As a member of the board of directors, Grant will help the nonprofit organization to pursue its mission of promoting public understanding and support for bioscience research. Founded in 1989, NCABR supports teacher education and bioscience research advocacy programs throughout North Carolina.



Grant, above, provides guided tours of the NIEHS animal facility for annual teacher workshops co-sponsored by NIEHS and NCABR. According to Wilkison, she is a favorite with the educators and consistently receives glowing reviews from participants. (Photo courtesy of Steve McCaw)

The group's members include representatives of academic, industry, government, hospital, nonprofit research, voluntary health and other nonprofit organizations united to help North Carolina residents better understand the science that so strongly influences the quality of their lives.

Grant will join three other scientists as new members on the board — Naina Bhasin, Ph.D., director of business and technology development at The Hamner Institutes of Health Sciences in Research Triangle Park; Stanley Faeth, Ph.D., professor and head of the biology department at the University of North Carolina at Greensboro; and Paul J. Gemperline, Ph.D., associate vice chancellor for research and graduate studies and the acting dean of graduate studies at East Carolina University in Greenville.

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NTP Leadership Looks Forward at Summer Board Meeting

By Eddy Ball

When the National Toxicology Program (NTP) Board of Scientific Counselors (BSC) met at NIEHS July 23–24, the group faced the usual order of business with reviews, reports, nominations and concepts, and interagency agreements ([see text box](#)).

Early in the meeting, members also learned of new developments on the horizon in regard to public health and communication of potential health risk, as the NTP enters its fourth decade and evolves to meet the challenge of the [NTP Vision for the 21st Century](#). The themes introduced in the first few hours of the meeting emerged repeatedly in discussions over the next day and a half.

The meeting opened with a welcome from BSC Chair Kenneth Portier, Ph.D., director of statistics for the American Cancer Society. NIEHS and NTP Director Linda Birnbaum, Ph.D., made the first presentation of the meeting with her welcome and report, which emphasized the integration of all parts of NIEHS and NTP in pursuit of the Institute's public health mission.

Much of Birnbaum's report was an update on her recent activities and initiatives, as she shared her thoughts "on where we're going in the next couple of months." She described searches for open leadership positions and plans to re-establish the Institute's office in Bethesda with at least three high-level liaisons — "one to the public health community, one to the toxicology community and one to the HHS [U.S. Department of Health and Human Services] community."

As part of her continuing efforts to increase participation and interaction with partners and stakeholders, Birnbaum told the BSC about a pending Memorandum of Understanding with the U.S. Environmental Protection Agency that "will allow us to have full collaboration and integration of some facilities... and other opportunities for sharing." Birnbaum said her emphasis on partnerships and outreach in [recent speaking engagements](#) at venues, such as the Toxicology Forum in Aspen, is part of her commitment to "more collaboration in strengthening environmental health research across the government."



Attending his first BSC meeting was Boston Biomedical Research Institute Senior Scientist James Sherley, M.D., Ph.D. Sherley was concerned that contextualizing toxicology results might mean a departure from the traditional NTP practice of "science reported exactly." (Photo courtesy of Steve McCaw)

Birnbaum also took the occasion to look even farther ahead into the future of toxicology and public health as she referred to her “new vision for NIEHS and NTP.” Practical implications for NTP include increased emphasis on integrating alternative testing with “gold-standard” NTP animal studies, early life exposure with the inclusion of gestational exposures in rat studies and determination of “internal dose” — as well as administered dose — for more meaningful cross-species extrapolation of potential adverse health effects.

NTP Associate Director John Bucher, Ph.D., followed Birnbaum with the “NTP Update” and more indications of new directions the agency will take in the future that reflect “the beginning stages of Linda’s commitment to reinvigorating the National Toxicology Program.” In his report, Bucher reviewed staffing changes, recent meetings, alternative testing (see related Science story on the latest [international expert panel report](#)), *Report on Carcinogens* expert panels and ongoing developments in response to the NTP report on bisphenol A.

Midway in his report, Bucher also addressed the question of interpreting findings of non-cancer studies — and the larger question of communicating risk in more useful ways for public health decision making as more and more data become publicly available from new testing platforms.

Making what he called “a shot across the bow... [and] an early-stage information item,” Bucher turned to what he admitted will clearly be “an exceptionally difficult challenge for our programs over the next years” — as NTP explores how best to contextualize its toxicity data beyond “under the conditions of this study.” Bucher said he foresees extended discussion among the agency’s staff and its advisors as NTP finds a responsible balance between informing of risk to public health and qualifying the results of individual studies.

“I don’t have a solution at this moment,” Bucher conceded. “We’re going to have put extraordinary effort into this.”



“Another emphasis we have is providing guidance for proper utilization of new types of information,” Birnbaum said of the challenges of integrating high-throughput screening information into toxicology testing. (Photo courtesy of Steve McCaw)



New member Elaine Faustman, Ph.D., of the University of Washington Center on Human Development and Disability, clearly enjoyed one of the meeting’s lighter moments. She expressed support for Birnbaum’s public health emphasis. (Photo courtesy of Steve McCaw)



Bucher gestured as he talked about finding a balance between a researcher’s obligation to acknowledge the limitations of toxicology studies and the public’s need for timely information about health risks. (Photo courtesy of Steve McCaw)



BSC member and private consultant Tracie Bunton, D.V.M., Ph.D., above, praised the design of the Absorption, Distribution, Metabolism and Excretion (ADME) contract as “very important — thinking at multiple steps rather than doing something because it’s been done that way for years and years.” (Photo courtesy of Steve McCaw)



Howard outlined the public health impact of National Center for Toxicological Research (NCTR) studies that have led to banning chemicals or effecting voluntary changes in production. (Photo courtesy of Steve McCaw)

Nominations and Concepts, Contract Concept Review and NIEHS/NTP Interagency Agreements

While the meeting began with an eye toward the future of NTP and NIEHS, the bulk of the meeting was devoted to the ongoing business of NTP (background materials posted [online](#)). Still, as the presenters and board members considered the nuts and bolts of operating an interagency effort, what Birnbaum and Bucher said about public health obligations helped inform the group’s discussions.

- **Nominations and Concepts**

After discussing and voting to accept recommendations on six compounds from the “Technical Reports Review Subcommittee Report of the February 25, 2009 Meeting,” presented by BSC member Raymond Novak, Ph.D., the group discussed new nominations for studies. NTP scientists presented the rationale and study design for research projects on alkylanilines, doxynivalenol, dong quai, indium tin oxide, *p*-chlorobenzotrifluoride and Tris(4-chlorophenyl)methane and Tris(4-chlorophenyl)methanol.

- **Contract Concept Review**

Speaking for NTP, Michael Cunningham, Ph.D., Cynthia Smith, Ph.D., and Ruth Lunn, Ph.D., presented information on existing and revised contracts. The BSC voted to approve contracts related to Investigative Absorption, Distribution, Metabolism and Excretion (ADME) Studies of Toxicants in NTP Animal Model Systems; Toxicology and Carcinogenicity Studies; and Report on Carcinogens Support.

- **Interagency Agreements**

The board heard a report on interagency agreements with the National Center for Toxicological Research (NCTR) and the National Institute for Occupational Safety and Health (NIOSH) by Bucher. The group also heard reports on studies supported through the agreements by NCTR scientist Paul Howard, Ph.D., and NIOSH scientists Mark Toraason, Ph.D., and Michael Luster, Ph.D.



"I see this program as expanding in the future," Toraason said of the NIEHS/NTP and National Institute for Occupational Safety and Health (NIOSH) interagency agreement. (Photo courtesy of Steve McCaw)



BSC member and New York University Professor George Friedman-Jiménez, M.D., Ph.D., was excited about Michael Luster's research at NIOSH and its translational implications for occupational health and medicine. (Photo courtesy of Steve McCaw)

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NIEHS Launches Intramural Awareness Campaign

By Eddy Ball

As part of a three-month NIH-wide campaign to raise the visibility of the Intramural Program, investigators in the NIEHS Division of Intramural Research (DIR) staffed a table at the Institute's cafeteria on July 20 and handed out nearly 75 promotional coffee mugs. It was the first outreach event at NIEHS for the NIH "I Am Intramural" initiative, which is gathering information and testimonials from scientists and staff for a new public Intramural Web site.

According to NIH organizers, the new Web site will be instrumental in helping NIH "bring 'the best and brightest' from all walks of life into the Intramural Program, make connections with the broader scientific community, enroll patients in clinical studies and account to taxpayers and Congress for the investment they make here."



Free coffee mugs helped catch the attention of people on their lunch break. (Photo courtesy of Steve McCaw)

Scientists, clinicians and professional staff can submit stories about their experiences in the NIH Intramural Program at the NIH ["I Am Intramural" Web site](#). Developers are looking for stories, photos and scientific images that clearly explain how Intramural research improves people's lives, showcase the talents of professionals at all stages of their careers, provide information on how the Intramural scientists are training the "next generation" of biomedical scientists, and promote participation in Intramural clinical research studies.

Staffing the table for the kick-off event was [NIEHS Intracellular Regulation Group](#) Research Fellow Xueqian (Shirley) Wang, Ph.D. Wang was joined later in the lunch period by her group's leader, [Principal Investigator David Miller, Ph.D.](#), campaign representative at NIEHS.

According to Miller, because of its diversity, NIEHS has a unique contribution to make to the new Web site, as well as a special need for raising public awareness of its new Clinical Research Unit.

Staffers at the booth invited passersby to take a complimentary mug and learn more about how they can contribute to the campaign. Among the visitors to the information table was Fordham University Professor of Chemistry in the Department of Natural Sciences [Joan Roberts, Ph.D.](#), who has spent the past 17 summers investigating light and human physiology with scientists in the NIEHS Laboratory of Pharmacology.

"I think it's a great idea," Roberts said as she promised to share her experiences at NIEHS and the way her summers here have benefited her students at Fordham. "I always emphasize to my students how important it is to communicate advanced scientific ideas in an accurate but understandable fashion — to get the information out of the ivory tower to the people it could one day benefit."



From left to right, NIEHS Comparative Genomics Group scientists Elena Braithwaite, Ph.D., Wendy Boyd, Ph.D., and Julie Rice listened as Wang explained how they can contribute to the new Web site. (Photo courtesy of Steve McCaw)



NIEHS Deputy Scientific Director Bill Schrader, Ph.D., left, and Principal Investigator Perry Blackshear, M.D., D.Phil., toasted the success of the campaign as Wang watched from behind the table. (Photo courtesy of Steve McCaw)



Toward the end of the lunchtime period, Wang, left, enjoyed the antics as Miller, center, made a show of handing NIEHS Acting Deputy Director Steve Kleeberger, Ph.D., a mug from the dwindling supply. (Photo courtesy of Steve McCaw)

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Superfund Holds Teacher Workshop on Water Quality

By Rebecca Wilson

Hundreds of middle and high school students will be learning about the latest advances in water quality research and remediation this academic year, thanks to the NIEHS-funded University of North Carolina at Chapel Hill (UNC-CH) Superfund Research Program (SRP). Their teachers attended the third Environmental Education Teacher Institute, “Environment & Health: Making Connections Through Water Quality Investigations,” co-hosted by the [UNC-CH SRP](#) in Salter Path, N.C. July 12–17.

The weeklong [workshop](#) was an opportunity for twenty three teachers to learn about environmental health, science and civics issues related to water quality in North Carolina. The workshop featured individual hands-on classroom sessions and field experiences led by UNC-CH professors and staff.

Science Educator [Dana Haine](#), a UNC-CH SRP staff member, conducted activities with teachers addressing several topics related to environmental health, including chemicals in the environment, toxicology, point and non-point source pollution, hazardous waste, the EPA’s Superfund Program, remediation, and environmental justice. Environmental microbiologist [Fred Pfaender, Ph.D.](#), joined meeting participants during a field trip to give a presentation about bioremediation.

As part of their professional development activities, the teachers completed exercises from the Focus on Risk Module by [Project Learning Tree](#), which includes a chapter that enabled them to investigate hazardous waste sites in their local community. They also viewed the *Frontline* documentary “[Poisoned Waters](#)” and discussed how to incorporate civic action into their science curriculum.

Teachers will be able to use the workshop materials to enhance their curriculums, taking water sampling and other activities back with them into the classroom. Sarah Lancaster, a middle school science teacher, said that the material would be helpful for planning lessons. “I feel like I just audited six graduate classes and left with materials developmentally appropriate for my middle school science students,” she noted. “So many of these activities and labs will provide wonderful opportunities for students to analyze, evaluate and synthesize crucial scientific information.”

(Rebecca Wilson is an environmental health information specialist for MDB, Inc., a contractor for the NIEHS Superfund Research Program and Worker Education and Training Program.)

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Teachers Mariel Meadows of Granite Falls Middle School, left, and Joanne Altendorf of Southwest Guilford High School, right, perform a serial dilution experiment at this year’s Environmental Education Teacher Institute. (Photo courtesy of Dana Haine, UNC)

SOT Holds Reception for Birnbaum

By Eddy Ball

The Society of Toxicology (SOT) honored its former president, NIEHS and National Toxicology Program (NTP) Director Linda Birnbaum, Ph.D., with a Capitol Hill reception on July 8 in Washington.

The group invited Birnbaum's colleagues and friends, members of Congress and their staff, the NIEHS Public Interest Partners and representatives from a number of organizations that have an interest in the work of NIEHS to the event, which was held in the new Capitol Visitor's Center. Mary Gant and Leanna Kelly, NIEHS Bethesda, assisted SOT with planning and invitations.

More than 120 people attended the reception, including SOT Council members President Cheryl Walker, Secretary Martin Philbert, Vice President-Elect Jon Cook, Peter Goering, Ronald Hines and Susan Borghoff. Former NIEHS leaders Bill and Joyce Martin, now working in Washington, were also guests.

A longtime friend and supporter of NIEHS, Congressman David Price (D-NC), was the congressional host. In his brief remarks, he talked about his long friendship with Birnbaum and the importance of NIEHS research. Congressmen James Moran (D-VA) and Henry Brown (R-SC) also attended along with staff from a number of congressional offices.

Representatives of the NIH, Food and Drug Administration, U.S. Environmental Protection Agency and Centers for Disease Control and Prevention's Agency for Toxic Substances and Disease Registry were at the event.

Representatives of non-government groups included David Jacobs, research director of the Center for Healthy Housing; Jay Feldman, executive director of Beyond Pesticides/National Coalition Against the Misuse of Pesticides; Janet Phoenix, NIEHS Partner; David Mallino, lobbyist for the Laborers Union; Ellie Collinson representing the Breast Cancer Fund; Diane Wood, president of the National Environmental Education Foundation; Susan Boa from the Harvard Center for Health and the Global Environment; and John Balbus, former chief health scientist with the Environmental Defense Fund who is now with George Washington University.



Joyce Martin, left, joined Walker, center, and Birnbaum for light conversation early in the evening. (Photo courtesy of SOT)



Birnbaum made a point of speaking individually with many of the attendees, including Congressman Moran, right. (Photo courtesy of SOT)



Well-wishers posed with the guest of honor. Shown, left to right, are Bill Martin, Walker, Price, Birnbaum, Moran and Joyce Martin. (Photo courtesy of SOT)



Several more of Birnbaum's friends and colleagues gathered for a photo opportunity. Shown, left to right, are Shawn Lamb of SOT, Walker, Balbus, Philbert, Joyce Martin, Bill Martin and Hines. (Photo courtesy of SOT)

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High School Researcher at Dartmouth Wins Award

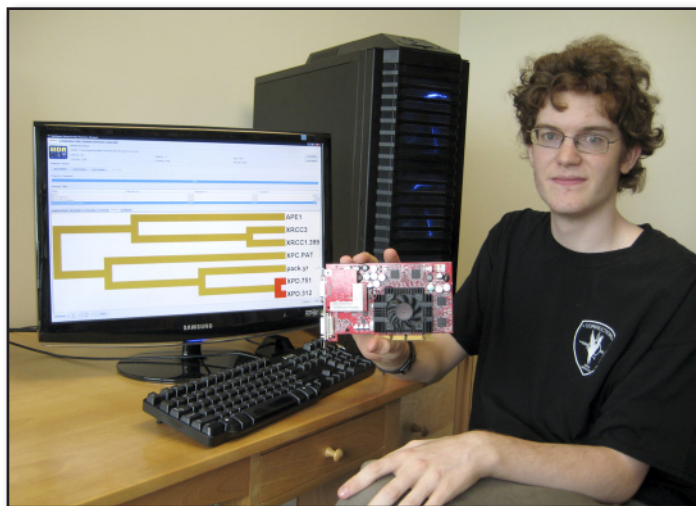
By Rebecca Wilson

Nick Sinnott-Armstrong, a high-school student who completed a summer research project in the Dartmouth College Superfund Research Program (SRP), took first prize for his work in a programming contest at the Genetic and Evolutionary Computation Conference (GECCO), held July 8–12 in Montreal.

Sinnott-Armstrong worked with Casey Green and Jason Moore, Ph.D., of the NIEHS-supported [Integrative Biology Core \(IBC\)](#) at Dartmouth to analyze and present epidemiological data using computer technology normally found in 3-D video games. He is the first author on a newly published [paper](#) reporting on the application in health research.

An advanced Graphical Processing Unit, or GPU, runs an adaptation of another Dartmouth innovation — a machine learning algorithm called [Multifactor Dimensionality Reduction \(MDR\)](#). MDR was built to detect and characterize interactions among various attributes to determine predictors of a particular outcome. It has been practically applied to the analysis of gene-environment interactions in genome-wide association studies.

The technology developed by the Core directly supports research efforts within the Dartmouth SRP. “The...GPU...reduces computational time by nearly 150-fold, compared to traditional computational methods,” said [Moore](#), who heads the IBC. “This significant speedup will greatly improve our ability to search through genomics datasets to identify those genes that interact with toxic metals and other environmental factors to influence susceptibility to common diseases such as cancer.”



When it comes to telling fellow students “How I Spent My Summer,” Sinnott-Armstrong, above, is sure to have one of the most interesting stories around. (Photo courtesy of Dartmouth College)

Citation: [Sinnott-Armstrong NA](#), [Greene CS](#), [Cancare F](#), [Moore JH](#). 2009. Accelerating epistasis analysis in human genetics with consumer graphics hardware. BMC Res Notes 2(1):149. [Epub ahead of print].

(Rebecca Wilson is an environmental health information specialist for MDB, Inc., a contractor for the NIEHS Superfund Research Program and Worker Education and Training Program.)

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Friends and Colleagues Mourn the Passing of K.C. Donnelly

By Eddy Ball

Following an extended battle with esophageal cancer, long-time Superfund Research Program (SRP) grantee K. C. Donnelly, Ph.D., died on July 1 in College Station, Texas at age 57. He is survived by his wife, Ruth, two sons and daughters-in-law, brother and sister.

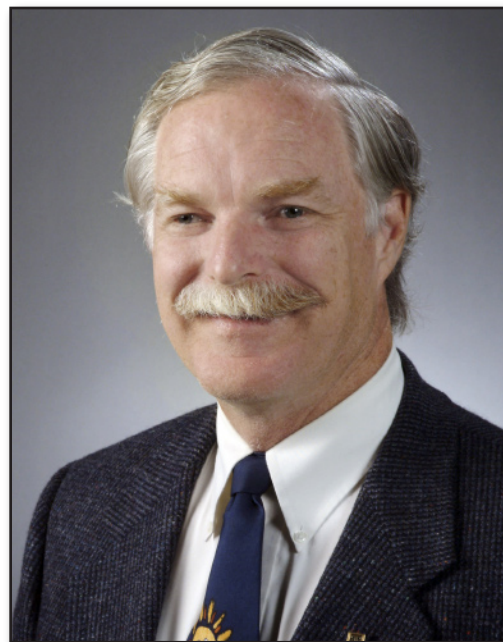
Donnelly served as a professor and head of the Environmental and Occupational Health Department in the School of Rural Public Health at the Texas A&M University (TAMU) System Health Science Center from 1999 through 2009. He was the associate director for the NIEHS-funded Superfund Basic Research Program at TAMU, held an appointment in the Department of Veterinary Integrated Biosciences at TAMU and was on the Executive Committee of the Interdisciplinary Faculty of Toxicology. Donnelly also held an appointment in the Department of Veterinary Integrated Biosciences at TAMU and was a member of the Federal Insecticide, Fungicide and Rodenticide Act Scientific Advisory Panel for the U.S. Environmental Protection Agency.

Donnelly's standing in the environmental health sciences community was reflected in the tributes of friends and colleagues as they learned of his death. In a statement from the TAMU Health Science Center, President Nancy W. Dickey, M.D., and Vice President for Academic Affairs Roderick McCallum, Ph.D., described Donnelly as "an idea man who finished the tasks at hand... [and] truly a remarkable colleague and friend."

When he learned of Donnelly's death, NIEHS SRP Director William Suk, Ph.D., observed that Donnelly "made significant contributions to the Program and NIEHS... [and] more importantly, at least to me, he was just about the nicest, kindest person I have ever had the privilege of knowing." Steve Safe, Ph.D., a long time faculty colleague and principal investigator of the TAMU Superfund Project, said, "K.C. was a superb colleague and friend who was dedicated to improving public health, particularly in underserved communities along the Texas-Mexico border and in other countries."

A memorial service for Donnelly was held July 5 at Aldersgate United Methodist Church in College Station, where he and his family were members.

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Toxicologist K.C. Donnelly (Photo courtesy of Melany Borsack and TAMU Health Science Center)

Science Notebook

Program Kicks Off Active Learning Format for Summer Interns

By Laura Hall

NIEHS [Summers of Discovery](#) students got their first taste of the program's new emphasis on active learning during a July 1 seminar on DNA repair, presented by NIEHS Principal Investigator [Thomas Kunkel, Ph.D.](#) Participants listened to brief talks that tied together three hands-on exercises.

Kunkel was implementing the program's new active learning format by having the students directly involved in their learning experience. The seminar provided lots of opportunities for interactive discussion and allowed students to perform the procedures they are studying, instead of passively listening to information and viewing slides during a lecture.

Leading up to the first exercise, Kunkel discussed the mechanisms of DNA polymerase, which he described as "the world's smallest word processor." To illustrate his point, he challenged the students to see if they could approach the accuracy of the polymerases using word processing software on the laptops at their tables.

Kunkel explained that the DNA polymerases in a human cell replicate the six billion "letters" in the human genome in a way roughly equivalent to copying 2,000 thick textbooks on a word processor in eight hours. He pointed out the "incredible accuracy" of the replicative DNA polymerases, which make less than one mistake per 10 million letters. In their exercise copying a 500-word paragraph, the students' own error rates ranged from 0 to as high as one in 20.

Accuracy during DNA replication is critical to human health, Kunkel continued. Mistakes result in mutations. The consequences can be harmful, with increased risk of cancer, degenerative disease, infertility, reduced immunity and even death. In some cases, however, Kunkel said mutations can perform a beneficial role, such as increasing selective advantage in evolution or promoting the development of normal immunity.

Pointing out that there are sixteen different DNA polymerases in the human cell, Kunkel gave the students the opportunity to determine the accuracy of three different DNA polymerases themselves using a laboratory method he developed in the early 1980s known as the [M13mp2 fidelity assay](#). The assay uses a reporter *lacZ*



Because active learning involves direct engagement to reinforce content, Kunkel kept the pace varied, alternating brief lectures with hands-on exercises. (Photo courtesy of Steve McCaw)



The environment of the room, with its tables for five or six students and normal lighting, was designed to be conducive for group interaction. (Photo courtesy of Steve McCaw)

gene in a DNA molecule copied by the test DNA polymerase. If the copy is accurate, the undisrupted gene will produce a blue bacteriophage plaque in a petri dish. If a polymerase error occurs, the resulting mutant will be evident in lighter blue and even colorless plaques.

The students used pressure-sensitive colony counters to count the number of mutated plaques, just as the members of the Kunkel laboratory do in their experiments. Kunkel said, “Research often gets down to the very mundane thing of counting M13 plaques on a petri dish and scoring for mutants.”

According to Diane Klotz, Ph.D., interim director of the NIEHS [Office of Fellows’ Career Development](#), David Armstrong, Ph.D., head of the Membrane Signaling Group, suggested integrating active learning into the student seminars. Armstrong, who was an observer at the seminar, said he learned about active learning from a 2008 [article](#) in *Science* and the 2007 book *Scientific Teaching* used in a program at the University of Wisconsin.

Klotz said she believes “the new format is working well and the events have piqued the interest of the summer interns.” As one of the students at the seminar, John Peart, noted, “The exercises helped me remember” the concepts of the presentation.



Kunkel, standing, explained how to read the agar plate to Alessandra Salgueiro. In the foreground, left to right, Josh Barzilai, John Beard, and Matthew Hunt worked out calculations. (Photo courtesy of Steve McCaw)



Jawara Allen, center, used one of the laptops for the word processing and mutant calculation exercises. (Photo courtesy of Steve McCaw)



In an exercise designed to be interactive and collaborative, Shashank Kommaraju, left, used one of the pressure colony counters to count mutants while Abhilash Guduru, right, examined an agar plate. (Photo courtesy of Steve McCaw)



Postdoctoral Fellow Mercedes Arana, Ph.D., showed John Beard, left, Alessandra Salgueiro, and Matthew Hunt, right, how to use the pressure colony counter. Two other fellows from the [Kunkel lab](#), Amy Abdulovic, Ph.D., and Jana Stone, Ph.D., also assisted at the seminar. (Photo courtesy of Steve McCaw)



Putting team science to action, student Jenessa Andrzejewski, center, conferred with other students at her table as they drew conclusions about the results of their data. (Photo courtesy of Steve McCaw)



Kunkel wrapped up his seminar with an explanation of the consequences of DNA polymerase infidelity and the implications for human health. (Photo courtesy of Steve McCaw)



Diane Klotz, above, who works with Debbie Wilson, the coordinator of the Summers of Discovery Program, was clearly pleased with the seminar format. "On average [this summer] we've had approximately 75-90 percent participation in the events, which is extraordinary." (Photo courtesy of Steve McCaw)

Highlights of the 2009 Summers of Discovery Program at NIEHS

The forty-six high school, undergraduate, and graduate school students in the 2009 NIEHS Summer of Discovery Program explore environmental science in a cutting-edge research setting. The students' experiences include working on a research project with mentors, science seminars incorporating active learning, and workshops on career development. The students also receive instruction in the practical aspects of working in a research laboratory — lab and radiation safety, animal handling, and computer and presentation skills.

On May 27, Linda Birnbaum, Ph.D., director of NIEHS and the National Toxicology Program (NTP) kicked off the 2009 program with an introduction to environmental research on the "bad actors" — environmental chemicals that detrimentally affect human health. In addition to giving an overview of historical and emerging human health risks from chemical exposures, Birnbaum discussed some of her own toxicology research.

In a July 15 seminar, Dori Germolec, Ph.D., a biologist in the Toxicology Branch, talked about allergic disease, with a focus on skin hypersensitivity and how potential chemical sensitizers are tested. Germolec discussed the need for alternative test methods and the role of [NTP and partner organizations](#). The students were asked to examine test data from four proposed alternate test methods and determine which ones they judged to be acceptable alternative methods.

On July 22, David Miller, Ph.D., principal investigator of the Intracellular Regulation Group, gave a seminar about how the body protects itself from many xenobiotic substances, including drugs, by way of the cytochrome P450 metabolizing enzymes (CYPs) and the ATP binding cassette efflux transporters, likening them to "chemists," "cops," and "bouncers." He explained how high xenobiotic concentrations could "overwhelm" the CYPs and transporters, leading to toxic drug-drug and drug-xenobiotic interactions. The students discussed possible causes of varying patient responses to therapeutic drugs in different scenarios.

The final seminar of the 2009 program on August 5 will be an introduction to epidemiology.

(Laura Hall is a biologist in the NIEHS Laboratory of Pharmacology currently on detail as a writer for the *Environmental Factor*.)

Public Comments Invited on Ocular Safety Testing Recommendations

By Debbie McCarley

The [National Toxicology Program \(NTP\)](#) [Interagency Center for the Evaluation of Alternative Toxicological Methods \(NICEATM\)](#), in conjunction with the [Interagency Coordinating Committee on the Validation of Alternative Methods \(ICCVAM\)](#), announced the availability of an independent scientific peer review panel report on alternative ocular safety testing methods and approaches and invited public comments in the July 13 issue of the *Federal Register*. The report endorses proposed recommendations by ICCVAM that are expected to improve the well-being and reduce the numbers of animals used to determine if consumer products and other chemicals can cause eye injuries. NICEATM asks that comments be submitted in response to the [request](#) electronically or in writing by August 28, 2009 ([see text box](#)).

The [meeting](#) of the panel of 22 expert scientists from six countries was held May 19–21 at the Consumer Product Safety Commission (CPSC) headquarters in Bethesda, Md., chaired by A. Wallace Hayes, Ph.D., of the Harvard University School of Public Health. The members reviewed new test methods and strategies proposed for determining if chemicals and substances may cause eye injuries. The panel was convened by NICEATM and ICCVAM to consider methods and strategies to further reduce animal use for eye safety testing and to avoid or minimize pain and distress in cases when animal use is necessary.

The panel recommended that pain-relieving drugs should always be used before any *in vivo* ocular irritancy testing. In addition, the group recommended an enhanced protocol of specific pain-relieving drugs and schedule of administration to effectively avoid or minimize discomfort. ICCVAM proposed several clinical conditions that could be used as humane endpoints to terminate ocular safety studies earlier than the typical 21-day observation period because they were considered sufficiently predictive of certain outcomes. The panel endorsed most of the proposed humane endpoints and agreed that they should be routinely used. The Panel also recommended that more detailed observations of the eye should be routinely conducted using a slit lamp biomicroscope to assess the severity of lesions, such as the depth of corneal injuries.

“The routine use of topical anesthetics and analgesics for ocular safety studies will ensure the most humane use of animals, and avoid pain and discomfort that might occur without the use of such agents,” said William Stokes, D.V.M., the executive director of ICCVAM and director of NICEATM, and an assistant surgeon



Seated left to right at the head of the table, are Stokes, Hayes and ICCVM Chair Marilyn Wind, Ph.D., of the CPSC. (Photo courtesy of NICEATM/ICCVAM)



Philippe Vanparys, Ph.D., left, managing director of the Belgium-based [Centre for Advanced Research and Development on Alternative Methods \(CARDAM\)](#), listens as James Jester, Ph.D., of the University of California-Irvine, makes a point about the cell biology of corneal wound healing. (Photo courtesy of NICEATM/ICCVAM)

general in the U.S. Public Health Service. “Importantly, since ocular testing is one of the four most common safety tests conducted, it will have a significant impact on the improvement of animal welfare.”

ICCVAM’s recommendations support the recently released NAS report, “Recognition and Alleviation of Pain and Distress in Laboratory Animals,” that calls for identification of humane endpoints and increased efforts to alleviate pain and distress.

The Panel also agreed with ICCVAM that two non-animal test methods, the Bovine Corneal Opacity and Permeability and the Cytosensor Microphysiometer® test methods, could be used in certain circumstances as screening tests to identify substances that do not cause sufficient eye irritation to trigger hazard labeling. These recommendations, if adopted by Federal agencies, are expected to further reduce animal use for ocular safety testing, and may potentially eliminate animal pain and distress in situations where animal testing is still required.

The panel evaluated the validation status of each of the proposed alternative test methods and applications according to established federal and international [criteria](#). The reviewers also commented on draft ICCVAM recommendations regarding the usefulness and limitations of each proposed test method and application.

The Panel’s report is available [online](#) or by request ([see text box](#)).

(Debbie McCarley is the Special Assistant to Rear Admiral William Stokes, D.V.M., D.A.C.L.A.M., director of the NTP Interagency Center for the Evaluation of Alternative Toxicological Methods.)

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The ICCVAM/NICEATM Mandate

Federal regulations require that new, revised and alternative test methods be determined to be valid for their proposed use before agencies can adopt them for regulatory purposes. ICCVAM, which has members from 15 Federal agencies, coordinates the technical evaluations of new, revised and alternative methods for regulatory safety testing of chemicals and products. ICCVAM will consider the Panel’s [report](#), along with comments from the public and its scientific advisory committee, in preparing final test method recommendations that will be forwarded to Federal agencies later this year. Acceptance of these recommendations by Federal agencies could result in fewer animals being required for identification of ocular hazards, as well as eliminating or minimizing pain and distress in cases where animal testing is still required.

In 2007, ICCVAM recommended two non-animal methods for use to identify substances that could cause permanent eye damage. These methods were accepted by Federal agencies and may now be used instead of conventional animal tests for certain regulatory testing purposes. The use of these two alternative test methods will likely reduce the use of live animals for eye safety testing by 10 percent or more and eliminate eye safety testing in animals of most substances likely to cause the most severe pain and discomfort. In June of this year, these two nonanimal methods, the Bovine Corneal Opacity and Permeability (BCOP) and isolated chicken eye (ICE), were adopted by the Organization for Economic Co-operation and Development (OECD). They can now be used in the 30-member countries to identify substances that may cause irreversible or severe eye damage without the use of live animals.

The goal of NICEATM and ICCVAM is to achieve the regulatory acceptance of alternative test methods that will benefit animal welfare by reducing, refining and replacing animal use — the 3Rs of alternative testing — and benefit public health by ensuring continued or improved protection of human and animal health and the environment.

Comments may be submitted electronically by [email](#) and the NICEATM/ICCVAM [Web site](#). Written comments should be addressed to the attention of NICEATM Director William Stokes, D.V.M., by fax (919-541-0947) or at the following addresses: NIEHS, P.O. Box 12233, Mail Stop: K2-16, Research Triangle Park, N.C.27709 (mail) or NIEHS, 530 Davis Drive, Room 2035, Durham, NC 27713 (courier).

Sun Exposure May Trigger Certain Autoimmune Diseases in Women

By Robin Mackar

Ultraviolet (UV) radiation from sunlight may be associated with the development of certain autoimmune diseases, particularly in women, according to a new study by researchers at the NIEHS.

“This study found that women who lived in areas with higher levels of UV exposure when they developed an autoimmune muscle disease called myositis were more likely to develop the form known as dermatomyositis, which weakens the muscles and causes distinctive rashes, instead of the form called polymyositis that does not have a rash,” said [Frederick W. Miller, M.D., Ph.D.](#), chief of the Environmental Autoimmunity Group, Program of Clinical Research, at NIEHS. “Although we have not shown a direct cause and effect link between UV exposure and this particular autoimmune disease, this study confirms the association between UV levels and the frequency of dermatomyositis that we found in a previous investigation,” said Miller.

The [study](#), published in the August issue of *Arthritis & Rheumatism*, is also the first to evaluate and find a possible UV radiation association in autoimmune diseases in women.



Miller's group works in the only NIEHS lab located in Bethesda, Md.. (Photo courtesy of Steve McCaw)

According to Miller, women are more likely than men to develop many autoimmune diseases, but the reasons for this have not been clear. “We only found the association between UV exposure and dermatomyositis in women and not in men, and it could be that inherent differences in how women and men respond to UV radiation may play a role in the development of certain autoimmune diseases,” said Miller. Miller also noted that other researchers have shown that female mice develop more skin inflammation after UV light exposure compared to male mice and these effects may be related to the new findings in dermatomyositis.

The study was designed to determine if there was a relationship between the level of UV exposure at the onset of the disease and the type of myositis and autoantibodies that people developed. Dermatomyositis and polymyositis are the two major forms of myositis and both are considered autoimmune diseases, in which the body's immune system attacks muscle or skin and sometimes other tissues. Dermatomyositis is typically accompanied by a distinctive reddish-purple rash on the upper eyelids or over the knuckles and is often made worse with sun exposure.

To conduct the study, the NIEHS researchers collaborated with myositis centers across the country that had seen 380 patients who had been diagnosed with dermatomyositis or polymyositis and determined their autoantibodies. “Patients with autoimmune diseases make a variety of autoantibodies that are unique to different conditions. One autoantibody specifically associated with dermatomyositis is called the anti-Mi-2 autoantibody and we know from our previous research that UV radiation increases levels of the Mi-2 protein that this autoantibody binds to,” said Miller.

In addition to finding an association between the level of UV radiation and the proportion of women who developed dermatomyositis compared to polymyositis, the researchers found an association between UV levels and the proportion of women with the anti-Mi-2 autoantibody. “More research is clearly needed to understand the potential links between UV radiation and the development of autoimmune diseases and autoantibodies in women,” said Miller.

“While the causes of autoimmune diseases are not known, we suspect from emerging research that they develop after one or more environmental exposures in genetically susceptible people,” said NIEHS Director Linda Birnbaum, Ph.D. “This study adds UV radiation to the growing list of environmental exposures possibly important in the development of autoimmune diseases.”

Citation: Love LA, Weinberg CR, McConaughy DR, Oddis CV, Medsger TA, Reveille JD, Arnett FC, Targoff IN, Miller FW. 2009. Ultraviolet radiation intensity predicts the relative distribution of dermatomyositis and anti-Mi-2 autoantibodies in women. *Arthritis Rheum* 60(8):2499–2504. [Epub ahead of print]

(Robin Mackar is the news director in the NIEHS Office of Communications and Public Liaison and a regular contributor to the *Environmental Factor*.)

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NIEHS Investigators Explore Biochemical Causes of Mitochondrial Disease

By Brian Chorley

A recent study published in the July 17 issue of the *Journal of Biological Chemistry* explored how certain DNA mutations may contribute to genesis and progression of mitochondrial diseases. NIEHS Principal Investigator [William Copeland, Ph.D.](#), and Postdoctoral Fellow, Rajesh Kasiviswanathan, Ph.D., led an effort to characterize these DNA mutations which are present in patients of Alper’s syndrome, an often fatal disease attributed to mitochondrial dysfunction. Their findings demonstrated that some of these mutations deleteriously impact mitochondrial DNA replication — a function critical for maintenance and activity of this important cellular organelle.

According to the NIEHS Laboratory of Molecular Genetics (LMG) researchers, the [study](#) represents the first structure-function analysis of its kind performed on what is known as the thumb subdomain of the mitochondrial DNA replication enzyme, polymerase gamma (pol γ), and offers insight into the effects of mutations in this region.

Copeland has dedicated his scientific career to uncovering the biochemical and genetic causes of mitochondrial abnormalities ([see text box](#)). A central player of many projects in Copeland’s laboratory is the DNA pol γ enzyme — the sole polymerase available in the mitochondria for replication of its DNA. A mutation within the gene encoding pol γ may lead to a cascade of downstream events, which can result in mitochondrial DNA depletion and, ultimately, mitochondrial-mediated disease. In a recent synopsis of his group’s research, Copeland explained, “There are currently more than 150 [single] mutations in the POLG gene that cause a wide spectrum of mitochondrial disease.... We have discovered more than 25 percent of these mutations and biochemically characterized the pol γ enzymes that harbor these disease alterations.”



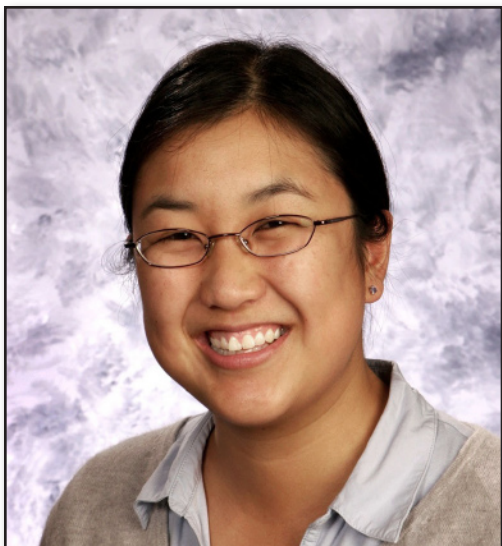
The study is Kasiviswanathan’s fourth publication as first author. (Photo courtesy of Steve McCaw)

In their current study, the researchers focused on 6 pol γ mutations linked to the mitochondrial disease Alper's syndrome. This rare inherited neurological disease typically affects young children who often do not live into their teens due to the cerebral degeneration associated with the disease. Recent work, spearheaded by the Copeland group, has linked pol γ mutations to Alper's syndrome, but only a handful of these mutations have been demonstrated to have direct biochemical effects on the function of the enzyme.

Using purified preparations of polymerases exhibiting these mutations, Copeland's laboratory assessed activity, DNA binding and mutation potential of these enzymes. The results both surprised the group and affirmed their predications. Some of the mutations linked to Alper's syndrome predictably abrogated polymerase activity and function, while other mutations caused only moderate biochemical alterations but were linked to severe disease symptoms. Copeland's explanation for the latter scenario is these mutations work in concert with other mutations which also alter proteins known to contribute to mitochondrial DNA replication leading to the development of Alper's. The exact nature of these interactions were unknown and the authors made it clear that more studies are needed to gain a better understanding of genomic replication in the mitochondria.

While there are no known cures or proven treatment for mitochondrial diseases, studies such as these will further basic understanding of genetic causes for these diseases. This basic understanding will undoubtedly spur therapeutic promise for the future.

In addition to Copeland and Kasiviswanathan, LMG Staff Scientist Matthew Longley, Ph.D., and former NIEHS Postdoctoral Fellow Sherine Chan, Ph.D., were coauthors on the paper.



Chan is now an assistant professor in the College of Pharmacy at the Medical University of South Carolina. (Photo courtesy of Steve McCaw)



Longley has collaborated with colleagues in the Copeland group and the NIEHS Laboratory of Structural Biology on more than 25 studies published since 1998. (Photo courtesy of Steve McCaw)



Copeland has been a leader in his field since establishing his lab at NIEHS in 1993. In 2007 he received the Mitochondria Research Society's Distinguished Service Award for service as its president in from 2005 to 2007. (Photo courtesy of Steve McCaw)

Mitochondrial Disease — Deficits in Energy Production

Mitochondrial disease is defined as a spectrum of ailments resulting from failure of mitochondrial function. Commonly referred to as the “powerhouse of the cell,” the mitochondria’s primary function is to supply cells with chemical energy. While mitochondrial disease can target practically any organ in the body, cells that require high amounts of energy, such as muscle, brain and nerve cells, are particularly vulnerable. Mitochondrial diseases typically afflict young children before the age of 10. However, adult onset of disease is now being diagnosed more frequently due to better recognition of symptoms and identification of genetic causes.

Mitochondrial diseases are unique because they can display maternal patterns of inheritance. In addition to nuclear-derived proteins whose genes display normal patterns of inheritance, mitochondria are also made up of proteins derived from their own DNA, which encodes 37 genes important for mitochondrial function. The female egg contributes mitochondrial DNA during zygote formation, where the sperm mitochondrial DNA is targeted for destruction. Because of this, any DNA mutation present in the egg’s mitochondria will be directly passed to offspring.

Direct mitochondrial diseases affect about 1 in every 2000 births, with about half developing in childhood and the other half presenting in adults. Mitochondrial deficits also have a secondary role in many other diseases, such as Parkinson’s Alzheimer’s, Huntington’s and diabetes. About ten percent of autistic children show biomarkers of mitochondrial disease.

Copeland explored additional aspects of mitochondrial diseases in a [review](#) published in 2008 in the *Annual Review of Medicine*.

Citation: [Kasiviswanathan R, Longley MJ, Chan SS, Copeland WC](#). 2009. Disease mutations in the human mitochondrial DNA polymerase thumb subdomain impart severe defects in mitochondrial DNA replication. *J Biol Chem* 284(29):19501-19510.

(Brian Chorley, Ph.D., is a postdoctoral fellow in the NIEHS Laboratory of Molecular Genetics Environmental Genomics Group.)

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Mouse Model Shows Early Symptoms of Parkinson’s Disease

By Negin Martin

In a new study funded in part by NIEHS and published in the June 24 issue of the *Journal of Neuroscience*, Emory University scientists unveiled a new mouse model with reduced monoamine storage capacity that manifests the early non-motor symptoms of Parkinson’s disease (PD). This engineered mouse model could offer insight into the early symptoms of PD and lead to the discovery of new avenues for early diagnosis and treatment of the disease — a progressive neurodegenerative condition caused by disruption of the dopamine system that devastates one million Americans each year.

Currently, there are no restorative cures or preventive measures available for PD patients. In many cases, early detection and adjunctive treatment can significantly improve quality of life and potentially delay disease progression.

“These mice are very useful for studying the major non-motor symptoms of Parkinson’s because they have them together as a package,” explained lead investigator [Gary Miller, Ph.D.](#), in an interview following publication of the study. Miller is an associate professor in the departments of Environmental and Occupational Health in the Rollins School of Public Health and Neurology and Pharmacology in the School of Medicine at Emory University and principal investigator of the NIEHS-funded [Parkinson’s Disease Collaborative Environmental Research Center at Emory University](#).

The mouse strain engineered for the [study](#) lacks an integral membrane protein known as vesicular monoamine transporter 2 (VMAT2). Miller and his colleagues developed this mouse model to study how dysfunction of other monoamine system neurotransmitters, such as serotonin and norepinephrine, may contribute to the onset of PD.

VMAT2 transports monoamines — neuronal signal molecules such as dopamine, serotonin and norepinephrine — in a neuron. Absence of this protein led to the reduction of norepinephrine and serotonin levels in all regions of brains in 12- to 15-month old mice that were tested by the investigators. These mice are considered middle-aged to old since the life expectancy of mice is about 24 to 30 months. According to the researchers, the VMAT2 gene in mice is 92% identical to its counterpart gene in humans.

Researchers observed that VMAT2-deficient mice could not discriminate between scents as well as normal mice at an early age and that their olfactory function declined with age. Other distinguishing characteristics of these mice also seen in humans with PD were delayed gastric emptying, altered sleep latency, and anxiety-like and age-dependent depressive behaviors.

Interestingly, all of these characteristics are recognized as early-onset non-motor symptoms of PD in humans. Motor disturbances — tremors, rigidity of movement and lack of balance — appear after 70-80% of striatal dopamine has been lost in PD patients. The non-motor symptoms such as loss of the sense of smell, gastrointestinal abnormalities, sleep disturbances, anxiety and depression appear prior to the onset of movement disorders and are early warning signs of PD.

One of Miller’s graduate students in the Molecular and Systems Pharmacology Program at Emory University, Tonya Taylor, was first author on the study, which was co-authored by specialists from several departments in the School of Medicine. Taylor graduated from Duke University in 2005 with a degree in Chemistry. She was named a Neuroscience Scholar by the Society for Neuroscience.



First author Tonya Taylor is a recipient of a National Research Service Award from NIEHS. (Photo courtesy of Tonya Taylor and Emory University)



Principal investigator Gary Miller is shown in his laboratory at Emory. (Photo courtesy of Ann Borden, Emory University)

The interdisciplinary research team was supported by NIEHS [center](#) and [training](#) grants, along with funding from the National Science Foundation and Michael J. Fox Foundation.

Citation: Taylor TN, Caudle WM, Shepherd KR, Noorian A, Jackson CR, Iuvone PM, Weinshenker D, Greene JG, Miller GW. 2009. Nonmotor symptoms of Parkinson's disease revealed in an animal model with reduced monoamine storage capacity. J Neurosci 29(25):8103-8113.

(Negin Martin, Ph.D., is a biologist in the NIEHS Laboratory of Neurobiology Viral Vector Core Facility and a 2009 Science Communication Fellow with Environmental Health Sciences. She recently completed a postdoctoral fellowship with the NIEHS Membrane Signaling Group.)

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Child's IQ Can Be Affected by Mother's Exposure to Urban Air Pollutants

By Robin Mackar

A mother's exposure to urban air pollutants known as polycyclic aromatic hydrocarbons (PAHs) can adversely affect a child's intelligence quotient or IQ, a new study in the journal *Pediatrics* reports. PAHs are chemicals released into the air from the burning of coal, diesel, oil and gas, or other organic substances such as tobacco. In urban areas, motor vehicles are a major source of PAHs.

The [study](#), funded by NIEHS, the U.S. Environmental Protection Agency and several private foundations, found that children exposed to high levels of PAHs in New York City had full scale and verbal IQ scores that were 4.31 and 4.67 points lower than those of less exposed children. High PAH levels were defined as above the median of 2.26 nanograms per cubic meter (ng/m³). A difference of four points, which was the average seen in this study, could be educationally meaningful in terms of school success, as reflected, for example, in standardized testing and other measures of academic performance. However, the researchers point out that the effects may vary among individual children.

"This research clearly shows that environmental PAHs at levels encountered in an urban setting can adversely affect a child's IQ," said Linda Birnbaum, Ph.D., director of NIEHS. "This is the first study to report an association between PAH exposure and IQ, and it should serve as a warning bell to us all. We need to do more to prevent environmental exposures from harming our children."

The study was conducted by scientists from the Columbia University Center for Children's Environmental Health. It included children who were born to non-smoking black and Dominican-American women age 18 to 35 who resided in Washington Heights, Harlem or the South Bronx in New York. The children were followed from *in utero* to 5 years of age. The mothers wore personal air monitors during pregnancy to measure exposure to PAHs, and they responded to questionnaires.



Lead author Frederica Perera (Photo courtesy of Frederica Perera and the Columbia Center for Children's Environmental Health)

At 5 years of age, 249 children were given an intelligence test known as the Wechsler Preschool and Primary Scale of the Intelligence, which provides verbal, performance and full-scale IQ scores. The test is regarded as a well validated, reliable and sensitive instrument for assessing intelligence. The researchers developed models to calculate the associations between prenatal PAH exposure and IQ. They accounted for other factors such as second-hand smoke exposure, lead, mother's education and the quality of the home caretaking environment. Study participants exposed to air pollution levels below the average were designated as having low exposure, while those exposed to pollution levels above the median were identified as high exposure.

"The decrease in full-scale IQ score among the more exposed children is similar to that seen with low-level lead exposure," said lead author [Frederica P. Perera, Dr.P.H.](#), professor at Columbia's Mailman School of Public Health and director of the Columbia Center for Children's Environmental Health.

"This finding is of concern," said Perera. "IQ is an important predictor of future academic performance, and PAHs are widespread in urban environments and throughout the world. Fortunately, airborne PAH concentrations can be reduced through currently available controls, alternative energy sources and policy interventions."

Citation: [Perera FP, Li Z, Whyatt R, Hoepner L, Wang S, Camann D, Rauh V](#). 2009. Prenatal Airborne Polycyclic Aromatic Hydrocarbon Exposure and Child IQ at Age 5 Years. *Pediatrics* Jul 20. [Epub ahead of print]

(Robin Mackar is the news director in the NIEHS Office of Communications and Public Liaison and a regular contributor to the *Environmental Factor*.)

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New Treatment May Help with Side Effects of Chemotherapy

By Eddy Ball

A new study funded in part by NIEHS reports experimental findings that may help prevent a dangerous side effect of the widely used chemotherapeutic drug cisplatin. The findings, which were published in the June issue of *Cell Biology and Toxicology*, could one day offer hope for the estimated five to ten percent of cisplatin-treated patients who experience renal failure as a consequence of their treatment for lung, ovarian, testicular, bladder, and head and neck tumors.

The [study](#) was conducted by NIEHS grantee [Bruce Hammock, Ph.D.](#), of the University of California, Davis and a team of Texas A&M University (TAMU) researchers led by first author [Alan R. Parrish, Ph.D.](#) The investigators demonstrated that increasing serum levels of the fatty acid 12-(3-adamantan-1-yl-ureido)-dodecanoic acid (AUDA) effectively blocked an enzyme known as soluble epoxide hydrolase (sEH) that is implicated in the hypertensive and inflammatory effects of cisplatin in the kidneys of mice.



Hammock, above, is shown with the insect that began his odyssey from basic to translational research — the hungry caterpillar. Hammock has enjoyed NIEHS support for his research since his first grant in 1979. (Photo courtesy of Bruce Hammock and the University of California, Davis)

The treatment protocol involved injecting the *n*-butyl ester of the fatty acid (nbAUDA) in a vehicle solution into mice also treated with cisplatin. Because the treatment appears to be free of significant side effects, the protocol could give physicians an alternative to medications now in use that are not so benign.

According to the study's authors, this novel approach may represent the first significant advance in clinical management of acute renal failure since the development of dialysis.

Mice in the experiments included a control group and groups that received one of three treatment protocols — cisplatin alone, nbAUDA alone, or both. The researchers also injected a separate group of mice with the vehicle solution to determine that the vehicle by itself had no effect on AUDA levels. Blood samples were analyzed at regular intervals during the course of treatment for levels of AUDA and a marker of renal damage — blood urea nitrogen (BUN).

The researchers found that treatment with nbAUDA resulted in elevation of AUDA in serum and produced a significant, if not complete, reduction in BUN levels for the mice administered both nbAUDA and cisplatin compared to those injected with cisplatin alone. After euthanizing the mice, the investigators examined the animals' kidneys by histology. While almost complete loss of tubular structure was evident in the kidneys of cisplatin-only mice, "tubules from nbAUDA/cisplatin mice look remarkably normal," the researchers reported — similar to mice in the control and nbAUDA-alone groups.

Experiments with humans should produce similar results, the authors explained, since sEH "represents a single known gene product with over 90 percent homology between rodent and human." They added that the viability of sEH-deleted mice suggests that side effects from inhibition of the enzyme should be minimal.

Along with funding from the TAMU vice president for research and the National Heart, Lung and Blood Institute, the study was supported by grants from NIEHS for research on [hydrolytic enzymes](#) and [biomarkers of exposure to hazardous substances](#).

Citation: Parrish AR, Chen G, Burghardt RC, Watanabe T, Morisseau C, Hammock BD. 2009. Attenuation of cisplatin nephrotoxicity by inhibition of soluble epoxide hydrolase. *Cell Biol Toxicol* 25(3):217-225.

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From Caterpillars and Pesticides to Clinical Trials

This research on attenuating the side effects of cisplatin built on findings by Hammock and colleagues in several earlier studies of the effects of sEH inhibition on blood pressure, pain and inflammation (see November 2006 story "[Distinguished Lecturer Outlines Hypertension Breakthrough](#)").

In the early 1980s with funding from the NIEHS Superfund Research Program, Hammock began investigating the role of hydrolytic enzymes involved in the degradation of insect juvenile hormone, including esterases and epoxide hydrolases. His group then looked at the roles of similar enzymes in mammals, initially in search of ways to protect humans from the effects of pesticides. As his research progressed, however, Hammock discovered the potential benefits of inhibiting one of them — the soluble epoxide hydrolase — in the treatment of hypertension, pain and inflammation in mammals.

Blocking the enzyme has the effect of redirecting fatty acid metabolism away from the arachidonic acid pathway associated with inflammation and hypertension and has shown promise with several aspects of metabolic syndrome. A compound developed by Hammock to inhibit sEH, known as AR9281, was found to be safe and well tolerated in healthy volunteers and is currently undergoing Phase IIa [clinical trial](#) for treatment of diabetes.



Parrish, above, led the TAMU team on the study and was first author. (Photo courtesy of Melany Borshack and TAMU Health Sciences Center)

Combined Biomarkers Improve Accuracy of Prostate Cancer Detection

By Robin Arnette

According to data from 2004–2006, the [National Cancer Institute](#) estimates that one in six American men will be diagnosed with prostate cancer during their lifetime. Since early detection of the disease increases the likelihood of survival, physicians routinely use serum prostate specific antigen (PSA) screening and subsequent tissue biopsy to determine whether a patient has prostate cancer. However, recent [findings](#) from a team led by [NIEHS grantee Shuk-mei Ho, Ph.D.](#), suggest that a dual marker test comprised of α -methylacyl-CoA racemase (AMACR) and prostate cancer antigen 3 (PCA3) provides increased sensitivity and accuracy compared to PSA testing alone.

These promising results appeared in the June 2009 edition of *The Journal of Urology*. This study was the first to examine the applicability of the combined biomarkers in the detection of prostate cancer in urine.

[Ho](#), chair of the Department of Environmental Health at the University of Cincinnati Medical Center, knew that a percentage of men with elevated PSA levels in their blood — a key indicator of prostate cancer — also have negative biopsy results. Her goal was to develop a sensitive test that would prevent these patients from having to undergo repeated biopsies. “Not only will this assay save billions of dollars in unnecessary biopsies each year, but it will be particularly useful for men over 70 years old who have high PSA numbers, but negative biopsies,” Ho said. “Because of their advanced age, do we really want to subject them to continuous biopsies?”

AMACR regulates peroxisomal beta-oxidation of phytol-derived branch chain fatty acids and PCA3 is a noncoding mRNA that is only expressed in the kidney and prostate epithelial cells.

Previous studies from other laboratories determined that these and several other proteins were found in urine samples of patients with prostate cancer, and therefore had great potential as diagnostic markers for the disease.

For the study of the combined AMACR-PCA3 assay, 92 patients, 43 with prostate cancer and 49 without, were recruited from the urological clinic at the University of Cincinnati Medical Center. The patients gave urine samples after digital examination, but before receiving an ultrasound-guided prostate biopsy. Ho’s team isolated RNA, used reverse transcriptase to convert to cDNA and then subjected the samples to quantitative real time polymerase chain reaction (qRT-PCR). Ho used several statistical analysis tools to resolve the sensitivity and specificity of AMACR and PCA3 scores in urine.



Ho, above, has also studied the [epigenetic alterations](#) involved in the development of prostate cancer. (Photo courtesy of Shuk-mei Ho and the University of Cincinnati Medical Center)



First author Bin Ouyang, Ph.D., is a research associate with the Department of Environmental Health, University of Cincinnati Medical Center. (Photo courtesy of Shuk-mei Ho and the University of Cincinnati Medical Center)

AMACR alone had 70 percent sensitivity and 71 percent specificity, while PCA3 alone had 72 percent sensitivity and 59 percent specificity. However, using the two together increased the sensitivity to 81 percent and the specificity to 84 percent. In contrast, serum PSA readings indicated 77 percent sensitivity and 45 percent specificity. Because the urinary AMACR- PCA3 test was superior to the blood PSA test in detecting prostate cancer, Ho suggests that the dual marker could be used as a surveillance test after repeat negative prostate biopsies or as an adjuvant to the serum PSA test to improve prostate diagnosis.

Ho is currently continuing patient recruitment to generate a larger sample size for future testing. “If the AMACR-PCA3 screening method becomes a standard in the diagnosis of prostate cancer, it would have a profound effect on millions of men,” she said.

Citation: Ouyang B, Bracken B, Burke B, Chung E, Liang J, Ho SM. 2009. A duplex quantitative polymerase chain reaction assay based on quantification of alpha-methylacyl-CoA racemase transcripts and prostate cancer antigen 3 in urine sediments improved diagnostic accuracy for prostate cancer. *J Urol* 181(6):2508-2513.

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This Month in EHP

By Eddy Ball

The August issue of [Environmental Health Perspectives \(EHP\)](#) explores “The Future of Toxicity Testing” with a Focus article on the Tox21 partnership of the National Toxicology Program, the NIH Chemical Genomics Center and U.S. Environmental Protection Agency that seeks to transform toxicology testing for the 21st century. Addressing the “Ethics of Observational Research,” a Spheres of Influence feature examines the ethical issues of the investigator’s role in child observational research.

In a Health Policy commentary, University of California, Berkeley Program in Green Chemistry and Chemicals Policy researchers Michael Wilson, Ph.D., and Megan Schwarzman, M.D., examine U.S. chemicals policy and offer arguments for rebuilding the foundation of policy to advance new science, green chemistry and environmental health.

Highlights from the issue include the following studies:

- **Racial Differences in Paraoxonase-1** — Offering further evidence to support the hypothesis that racial differences in cardiovascular disease risk may be partly explained by differences in paraoxonase-1, a lactonase/hydrolase that associates with high-density lipoprotein (HDL) particles
- **Half-Lives of Persistent Organic Pollutants in Human Populations** — Applying a multi-individual pharmacokinetic model for clarifying the interpretation of human elimination half-lives of persistent organic pollutants derived from cross-sectional trend data and estimating these values using data collected in post-ban situations



<http://twitter.com/ehponline>



- **Age of Greatest Susceptibility to Lead Exposure** — Using modeling data to demonstrate that blood lead (BPb) levels at six years of age may have a stronger impact on cognitive and behavioral development than BPb at two years of age and suggesting that BPb be included in diagnostic evaluations of school-age children with cognitive or behavioral problems

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David Sinclair to Present Distinguished Lecture August 11

By Eddy Ball

The 2008-2009 NIEHS Distinguished Lecture Series will conclude August 11 with a talk by Harvard University molecular geneticist David Sinclair, Ph.D. Sinclair's lecture on "Pathways That Control the Pace of Aging and Disease: Prospects for New Medicines" will begin at 11:00 a.m. in Rodbell Auditorium and be hosted by NIEHS Mammalian Aging Group Principal Investigator [Xiaoling Li, Ph.D.](#)

[Sinclair](#) is a professor of Pathology and co-director of the Paul F. Glenn Laboratories for the Biological Mechanisms of Aging at the Harvard University Medical School. Like Li, Sinclair studies the regulatory proteins known as sirtuins. He is especially interested in the interaction between their ortholog in humans, *SIRT1*, and calorie restriction in regulating mammalian lifespan.

His group has investigated the role of sirtuins in several models, including yeast, *C. elegans*, mammalian cell culture and rodents. Using an interdisciplinary approach in these studies, his group has applied results to develop engineered small molecules that can activate mammalian sirtuins *in vivo*, with a view to developing drugs to treat the diseases of aging and promote cell survival and recovery following an injury.

As well as being a leading investigator in his field, Sinclair is also an accomplished communicator of his science. He appeared on the Public Broadcasting Service show [Charlie Rose](#) in 2006 discussing his highly publicized [study](#) on the anti-aging red-wine compound resveratrol. His [article](#) in the July 2009 issue of the on-line magazine *SEED* offers a reader-friendly introduction to his work.

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Upcoming Distinguished Lecturer David Sinclair (Photo courtesy of David Sinclair and Harvard University)

Extramural Update

Hazmat Training Funding Opportunity Announcements

Pursuant to its role under the Superfund Amendments and Reauthorization Act of 1986 (SARA), on July 9 the [NIEHS Worker Education and Training Program](#) issued Requests for Applications (RFAs) for two new funding opportunity announcements (FOAs)—Hazardous Materials Worker Health and Safety Training (RFA-ES-09-004) and Hazmat Training at Department of Energy (DOE) Nuclear Weapons Complex (RFA-ES-09-003). For both RFAs, the due date for letters of intent is October 23, 2009, and applications are due November 23, 2009.

Section 126(g) of SARA authorizes an assistance program for the training and education of workers engaged in activities related to hazardous waste generation, removal, containment, transportation and emergency response. Congress assigned responsibility for administering this program to the NIEHS.

- [Hazardous Materials Worker Health and Safety Training \(U45\)](#)

The major objective of this solicitation is to prevent work-related harm by assisting in the training of workers in how best to protect themselves and their communities from exposure to hazardous materials encountered during hazardous waste operations, hazardous materials transportation, environmental restoration of contaminated facilities or chemical emergency response. A variety of sites, such as those involved with chemical waste clean up and remedial action and transportation-related chemical emergency response, may pose severe health and safety concerns to workers and the surrounding communities. These sites are often characterized by the multiplicity of substances present, the presence of unknown substances and the general uncontrolled condition of the site. A major goal of this program is to provide assistance to organizations in developing their institutional competency to provide appropriate model training and education programs to workers exposed to hazardous materials and waste.

This FOA lists three distinct program areas — Hazardous Waste Worker Training Program, Minority Worker Training Program, and the Hazmat Disaster Preparedness Training Program. A special [website](#) provides important background reports and other information about the three program areas.

- [Hazmat Training at DOE Nuclear Weapons Complex \(U45\)](#)

The major objective of this solicitation is to prevent work-related harm by assisting in the training and education of workers in the DOE nuclear weapons complex. Safety and health training will transmit skills and knowledge to workers in how best to protect themselves and their communities from exposure to hazardous materials encountered during hazardous waste operations, facility decommissioning and decontamination, hazardous materials transportation, environmental restoration of contaminated facilities or chemical emergency response. Currently, tens of thousands of DOE employees require safety and health training to help reduce the risk of their being exposed in the course of their work to hazardous materials and hazardous waste products.

For further information about the announcements, contact [Joseph Hughes](#), [Sharon Beard](#) or [Ted Outwater](#).

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Workers are shown learning how to use protective clothing and devices to avoid unnecessary exposures to hazardous materials. (Archive photo courtesy of SRA)

Extramural Papers of the Month

By Jerry Phelps



Read the current Superfund Research Program [Research Brief](#). New issues are published on the first Wednesday of each month.

- [HLA-DR4 – Possible Risk Gene for Autism](#)
- [Endocrine Society Position Statement on Endocrine Disruptors](#)
- [Bisphenol A Study Shows Reproductive Health Effects](#)
- [New Method May Accelerate Drug Discovery for Parkinson's](#)

HLA-DR4 – Possible Risk Gene for Autism

NIEHS-sponsored scientists report the discovery of a gene that may be involved in autism. The gene, known as HLA-DR4, is unique in that it acts in the mothers of children with autism disorder instead of acting in the children themselves. There are reports of about 30 such maternally acting or teratogenic genes.

The team genotyped members of 31 families for HLA-DR4. Children with autism were tested using a standard diagnostic psychological exam to confirm their condition. The results of the study led to the conclusion that HLA-DR4 is indeed a teratogenic gene and support the possibility of an immune component in the pathogenesis of autism.

The authors concluded that the gene could contribute to a subset of autism cases by interacting with other risk alleles or environmental factors to perturb pathways affecting brain development. They called for additional studies to address the causes of the development of autism that could lead to new interventions to prevent and treat the disorder.

Citation: [Johnson WG](#), [Buyske S](#), [Mars AE](#), [Sreenath M](#), [Stenroos ES](#), [Williams TA](#), [Stein R](#), [Lambert GH](#). 2009. HLA-DR4 as a risk allele for autism acting in mothers of probands possibly during pregnancy. *Arch Pediatr Adolesc Med* 163(6):542-546.

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Endocrine Society Position Statement on Endocrine Disruptors

In its first ever position statement, the Endocrine Society released a report outlining the public health concerns about exposure to endocrine disrupting chemicals and proposed a series of recommendations for revising current and generating new public-health related policies. The report states that the Society is concerned that the public may be at risk for exposure to endocrine disruptors because potential health effects are being overlooked in developing guidelines and regulations.

Endocrine disruptors are man-made compounds and substances in the environment that interfere with hormone production and action and metabolism, resulting in adverse health effects in a host of biological processes and systems in humans and wildlife. While stressing that it does not support alarmist action, the Society does support information dissemination on sources of exposure, potential health effects and preventive actions that can be taken to protect the American public from potential harm.

Recommendations in the report include centralized regulatory oversight of endocrine disrupting chemicals, policy development and research recommendations by a collaborative group of endocrinologists, toxicologists, epidemiologists and policy makers. The report also recommends the application of the precautionary principle to endocrine disrupting chemicals and the application of high-throughput research to test and identify many chemicals for endocrine disrupting activity.

Citation: [Diamanti-Kandarakis E, Bourguignon JP, Giudice LC, Hauser R, Prins GS, Soto AM, Zoeller RT, Gore AC. 2009. Endocrine-disrupting chemicals: An Endocrine Society scientific statement. Endocr Rev 30\(4\):293-342.](#)

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Bisphenol A Study Shows Reproductive Health Effects

New research results suggest that bisphenol A (BPA) significantly affects reproductive health at levels that are the same or lower than those currently considered to be too low to produce adverse effects. The research was conducted by Heather B. Patisaul, Ph.D., an NIEHS Outstanding New Environmental Scientist grantee.

BPA is a chemical used to harden many plastics in everyday food and beverage containers such as baby bottles, food can liners, water bottles and many other products. It is widely suspected of being an endocrine disrupting chemical.

The research team exposed female laboratory rats to 50 micrograms per kilogram of body weight in their first four days of life. The rats developed puberty earlier than their unexposed litter mates, significant ovarian malformations and premature loss of estrus. The dose is significant on a policy level because the EPA considers 50 micrograms per kilogram to be the human no-effect level.

Many states and municipalities have banned BPA totally or in products designated for children. Canada has announced plans to completely ban the chemical and has labeled it a toxin. Currently, there are bills in the U.S. House of Representatives and the Senate to ban the chemical in all food and beverage containers. This research may add evidence to support banning the chemical or restricting its use.

Citation: [Patisaul HB, Adewale HB. 2009. Long-term effects of environmental endocrine disruptors on reproductive physiology and behavior. Front Behav Neurosci 3:10. \[Epub ahead of print.\] doi:10.3389/neuro.08.010.2009.](#)

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New Method May Accelerate Drug Discovery for Parkinson's

A multi-center collaborative research effort partially funded by NIEHS has developed a rapid, inexpensive drug-screening method that could be used by drug developers to target Parkinson's as well as other debilitating diseases. The technique uses yeast to screen potential compounds, cutting the testing time to a few weeks.

Drug discovery is a long, difficult process requiring identification and synthesis of potential compounds, screening of compounds with expensive assays and definition of the structure of the compounds. Typically at the end of this months-long process, less than one per cent of the original compounds are deemed worthy of further testing in living cells.

The new method takes advantage of cyclic peptides that are capable of targeting the protein-protein interactions found in almost all cellular processes. Cyclic peptides are able to bind to proteins in smaller spaces where traditional drugs cannot. Using a yeast model of Parkinson's, the research team identified two cyclic peptides that were able to prevent dopaminergic neuron loss in the model. Once these peptides were sequenced, the team found that only the first four amino acids were necessary for the peptide to work. This four amino acid motif is similar to some important biochemical structures including molecules with oxidation or reduction properties and molecules that bind to metals.

Citation: [Kritzer JA, Hamamichi S, McCaffery JM, Santagata S, Naumann TA, Caldwell KA, Caldwell GA, Lindquist S. 2009. Rapid selection of cyclic peptides that reduce \$\alpha\$ -synuclein toxicity in yeast and animal models. Nat Chem Biol, doi:10.1038/nchembio.193.](#)

(Jerry Phelps is a program analyst in the NIEHS Division of Extramural Research and Training. Each month, he contributes summaries of extramural papers to the *Environmental Factor*.)

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Intramural Papers of the Month

By Robin Arnette and Laura Hall

- [Multivitamin Intake Is Associated with Longer Telomeres](#)
- [Pesticides Are Associated With Allergic Asthma in Male Farmers](#)
- [A Missense Mutation in *repro32* Mutant Male Mice Causes Infertility](#)
- [Elucidation of the Cu,Zn-Superoxide Dismutase Peroxide Cycle](#)

Multivitamin Intake Is Associated with Longer Telomeres

Telomeres, comprised of a repeated DNA sequence (TTAGGG) and proteins that occur at chromosome ends, prevent chromosomal damage and degradation. Because telomere length decreases during each cycle of cell division, it has been linked to a higher risk of several chronic diseases and mortality. Researchers in the field have proposed that shortened telomeres might be associated with accelerated “human aging.”

Investigators from NIEHS and the University of Utah have determined that multivitamin use is associated with longer telomeres in women. This examination is the first epidemiologic link between multivitamin consumption and longer telomeres.

The research team analyzed leukocyte DNA samples from participants in the [NIEHS Sister Study](#), a prospective cohort of healthy sisters of breast cancer patients. Team members used quantitative polymerase chain reaction (PCR) to measure the relative length of leukocyte telomeres and combined the data with participant information regarding the type, frequency and duration of multivitamin intake.

The age of these women ranged from 35 to 74 at the time of blood collection. The investigators found that on average, daily multivitamin users had 5.1 percent longer telomeres than non-users. The findings also corroborated

preliminary experimental evidence from others that vitamins C and E may protect telomeres *in vitro*. The analysis took into account known or suspected factors that were associated with telomere length such as age, smoking and perceived stress, but could not rule out potential impact from other unmeasured lifestyle factors.

Citation: Xu Q, Parks CG, DeRoo LA, Cawthon RM, Sandler DP, Chen H. 2009. Multivitamin use and telomere length in women. *Am J Clin Nutr* 89(6):1857-1863.

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Pesticides Are Associated With Allergic Asthma in Male Farmers

Using data from the [Agricultural Health Study \(AHS\)](#), researchers from NIEHS, the National Institute for Occupational Safety and Health (NIOSH) and the National Cancer Institute (NCI) have concluded that specific pesticides are associated with allergic asthma and that self-reported high pesticide exposure events (HPEE) are associated with both allergic and non-allergic asthma.

Enrolled between 1993 and 1997, the AHS is a prospective cohort of pesticide applicators and their spouses in Iowa and North Carolina. Fifty-two thousand licensed private pesticide applicators were enrolled in the AHS, but the analysis for this publication was limited to the 19,704 male farmers who completed both the initial and follow-up questionnaires. The questionnaires provided a complete medical history and information about smoking habits, body mass, respiratory and allergic symptoms, other respiratory illnesses and farming practices. The team members' goal was to evaluate the lifetime use of 48 pesticides and the prevalence of adult-onset asthma.

A history of a high pesticide exposure event doubled the rates of allergic and non-allergic asthma. Out of the 48 pesticides, 12 were associated with allergic asthma, with five exhibiting significant exposure-response trends: coumaphos, heptachlor, parathion, 80/20 mix (carbon tetrachloride/carbon disulfide) and ethylene dibromide. Four additional pesticides were associated with non-allergic asthma, with DDT having the strongest effect estimate.

Citation: Hoppin JA, Umbach DM, London SJ, Henneberger PK, Kullman GJ, Coble J, Alavanja MC, Beane Freeman LE, Sandler DP. 2009. Pesticide use and adult-onset asthma among male farmers in the Agricultural Health Study. *Eur Respir J* June 18. [Epub ahead of print]

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A Missense Mutation in *repro32* Mutant Male Mice Causes Infertility

Investigators at NIEHS, in collaboration with the researchers who created the *repro32* N-ethyl-N-nitrosourea (ENU)-induced mutated mouse line at the Jackson Laboratory in Bar Harbor, Maine, have determined that a missense mutation in the “capping protein muscle Z-line alpha 3” (*Capza3*) gene is responsible for abnormal spermiogenesis and a decrease in sperm production in *repro32* homozygous mutant mice. The CAPZA3 protein is a filamentous actin (F-actin) regulatory protein that likely forms a heterodimer with the sperm-specific variant CAPZB3 in order to regulate F-actin dynamics.

Male *repro32* mutant mice produce sperm that have irregularly-shaped heads and poor motility. Because the mutant sperm are unable to shed excess cytoplasm from the middle piece of the flagellum during spermiogenesis, a bag of cytoplasm encases both the abnormally developed flagellum and the sperm head.

The research team demonstrated that F-actin is involved in the development of normal sperm and that the abnormalities seen in the mutant sperm were due to the inability of CAPZA3 and F-actin to organize properly. This disorganization was caused by an N-terminal missense mutation in *Capza3*. The data indicate that CAPZA3 is required for the maintenance of male fertility in the mouse and possibly other mammalian species.

Citation: [Geyer CB](#), [Inselman AL](#), [Sunman JA](#), [Bornstein S](#), [Handel MA](#), [Eddy EM](#). 2009. A missense mutation in the *Capza3* gene and disruption of F-actin organization in spermatids of *repro32* infertile male mice. *Dev Biol* 330(1):142-152.

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Elucidation of the Cu,Zn-Superoxide Dismutase Peroxide Cycle

NIEHS researchers have shown that peroxymonocarbonate (HOOCO_2^-) is a key intermediate in the Cu,Zn-superoxide dismutase (SOD1) peroxidase cycle and a precursor of carbonate radical anions. This finding discounts the assumption that SOD1 involves the formation of hypervalent metal states similar to those in the heme-peroxidase catalytic mechanism.

SOD1 is an enzyme found in mammalian cells and tissues that protects them against damage generated by superoxide anion and other oxygen free radicals. SOD1 peroxidase activity has been proposed to be involved in the development of amyotrophic lateral sclerosis (ALS), a motor neuron disease that leads to progressive paralysis and death. Results indicate that the carbonate radical production from the peroxymonocarbonate intermediated SOD1 peroxidase cycle would not be sufficient at physiological pH to be a main contributor to the development of ALS.

The authors used electron paramagnetic resonance (EPR) to show that the rate limiting first step in the SOD1 peroxidase cycle uses the hydroxide anion (HOO^-) to reduce SOD1-Cu(II) to SOD1-Cu(I). Nuclear magnetic resonance (NMR) and EPR studies confirmed that HOO^- and carbon dioxide (CO_2), combine to form HOOCO_2^- . NMR studies established peroxymonocarbonate as the main substrate for the SOD1-Cu(I) oxidative conversion back to SOD1-Cu(II) having an estimated second-order rate constant 10 times higher than that of hydrogen peroxide (H_2O_2).

Citation: [Bonini MG](#), [Gabel SA](#), [Rangelova K](#), [Stadler K](#), [Deroose EF](#), [London RE](#), [Mason RP](#). 2009. Direct magnetic resonance evidence for peroxymonocarbonate involvement in the cu,zn-superoxide dismutase peroxidase catalytic cycle. *J Biol Chem* 284(21):14618-14627.

(Laura Hall is a biologist in the NIEHS Laboratory of Pharmacology currently on detail as a writer for the *Environmental Factor*.)

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Inside the Institute

Community Support Aids Green Science Camp

By Laura Hall

The Durham Alumnae Chapter of Delta Sigma Theta Sorority provided a fun-filled day for children and adults with a focus on green science at the fourth annual Science and Everyday Experiences (SEE) day camp on July 11. Along with the sorority sisters and community volunteers, many NIEHS employees and retirees volunteered their time to assist in instructing thirty Durham Public School fourth- to eighth- grade children in science and math activities.

This year's camp activities focused on green issues, emphasizing alternative energy solutions. Dick Sloane of NIEHS gave a demonstration on recycling and composting. Walter Weathers of the U.S. Environmental Protection Agency (EPA) explained the operation of solar panels. The children learned about electric, solar and wind energy.

In some of their activities, the children made batteries using fruits and vegetables, fabricated solar ovens from pizza boxes to cook s'mores, engineered an anemometer from paper cups to measure wind speed and simulated air transportation by using balloons, fishing lines and straws to understand how the force of air can be used to propel a vehicle. The materials used in all the children's activities were everyday items that could be found at home.

Parents were also able to participate with an informational workshop and hands-on science activities. The adult program was organized by Marian Johnson-Thompson, Ph.D., who recently retired from her position as NIEHS director of Education and Biomedical Research Development and Sandra White, Ph.D., a North Carolina Central University (NCCU) professor and wife of former NIEHS Director Ken Olden, Ph.D.



"Science is everywhere," said Sharon Beard, echoing a theme of the summer camp. Beard is chair of the Durham SEE and an NIEHS industrial hygienist in the Worker Education and Training Branch. (Photo by Laura Hall)



SEE campers posed for a group photo at the start of the fourth annual SEE Summer Camp. (Photo courtesy of Veronica Godfrey)

In the parent workshop, the adults heard several speakers who informed them of the opportunities available to children interested in math and science. The talks covered special high school curricula programs available for North Carolina children within the local area and across the state, educational enrichment programs, and how to advocate for healthy food and exercise in schools.

The talks were well received by the parents in the audience. “Very interesting,” remarked Tahra McLaughlin. “I wasn’t expecting this wealth of knowledge.” Participant Moses Best said the talks offered “very exciting information.” The adults also had a tremendous time in their interactive science activities, making DNA necklaces and solving puzzles.

The camp was almost derailed by the [theft](#) of copper piping from the air conditioning units at the Durham Alumnae Delta House in Durham. As an alternative site for the camp, Rhonda Parker, director of Durham Parks and Recreation, offered the use of the W. D. Hill Recreation Center. Hedy Echard, one of the sorority members, commented that the offers for alternate sites were an example of “community support generated at the last moment.”

The children barely noticed. They began their day with breakfast at the new site and a welcome by Deloris B. Hargrow, president of the Durham Alumnae Chapter, followed by a camp overview by Sharon Beard, NIEHS industrial hygienist. Then Shawn Jeter, an NIEHS technical information specialist who is also an aerobics instructor, led the children in physical exercises.

[SEE](#) is a national initiative of [Delta Sigma Theta Sorority](#) to encourage African-American children to gain competency and interest in science, mathematics and technology, by involving them in hands-on science activities that are fun and thought provoking. These activities demonstrate to the children that people use science and math every day.

(Laura Hall is a biologist in the NIEHS Laboratory of Pharmacology currently on detail as a writer for the *Environmental Factor*.)

Community Supports SEE with Volunteers and Donations

A number of participating organizations helped make this year’s SEE camp a success. They include the Delta Research and Educational Foundation, Burroughs Wellcome Fund Science Enrichment Program, Durham Parks and Recreation, cSc Sheet Metal, California Pizza Kitchen, U.S. EPA, along with the leadership of the Durham Alumnae Chapter of Delta Sigma Theta, Delta Sigma Theta Sorority, Inc., and NIEHS.

Speakers in the adult workshop included educators from the area:

- Tonya Peele, certified wellness coach and consultant for [Parents Promoting Wellness](#) program, on health food and exercise in schools.
- Sandra White, Ph.D., director of the NCCU Center for Science, Math and Technology Education, on the [Students Making Another Science Success Story \(SMASSS\)](#) program for seventh through 10th grades.
- Joan Barber, Ph.D., vice chancellor for student life at the [North Carolina School of Science and Mathematics](#), on entrance requirements.
- Diane Affleck, assistant director for Mathematics and Science Education Network (MSEN) at the University of North Carolina at Chapel Hill, on the North Carolina [MSEN Pre College program](#) for sixth through 12th grades — an enrichment instruction program in the Raleigh, Durham, Chapel Hill and Orange County area.
- Natasha Goodwin, dean of students for the [Josephine Dobbs Clement Early College High School](#), on the rigorous high school program that includes college courses at NCCU.
- Kenneth A. Cutler, director of the [NC Project SEED](#) program, on opportunities for talented disadvantaged North Carolina high school students to pursue graduate and professional school degrees in chemistry-related science disciplines.



Joan Packenham, Ph.D., standing left, SEE Co-Chair and director of the NIEHS Office of Human Research Compliance and NIEHS Postdoctoral Fellow Undi Hoffler, Ph.D., standing center, explained principles of electricity and how to make batteries from fruits and vegetables. (Photo by Laura Hall)



Lauren Davis, Ph.D., right, taught sixth through eighth graders how to set up their solar ovens. Davis is an assistant professor in the Department of Industrial and Systems Engineering at North Carolina Agricultural and Technical State University. (Photo by Laura Hall)



Dick Sloane, NIEHS Employee Services Specialist, discussed the value of recycling. (Photo by Laura Hall)



Sandra White, left, poured liquid for parents Tammi Hayes, center, and Lisa Corbett to use in one of the adult science activities. (Photo by Laura Hall)



NIEHS volunteers at the 2009 SEE camp shown left to right are Joan Packenham, Marian Johnson-Thompson, Undi Hoffler, Elena Braithwaite, Danielle Watt, Milele Bynum, Mwenda Kudumu, and Sharon Beard. Not shown are NIEHS volunteers and supporters VeeVee Shropshire, Charletta Fowler, Dick Sloane, Shawn Jeter, Veronica Godfrey and Kimberly Gray. (Photo by Laura Hall)

Wilcox Wows the Crowd at Science Café

By Laura Hall

Speaking at the Broad Street Café in Durham, N.C. on July 14, NIEHS epidemiologist Allen Wilcox, M.D., Ph.D., gave an informal talk on human fertility to a capacity audience made up largely of non-scientists. The talk was one of the Science Café's "Periodic Tables" events organized by the Museum of Life and Science in Durham.

Science Café is a venue that brings together people from all walks of life to discuss a broad range of current issues related to science, engineering and mathematics. The program called "[Periodic Tables](#)" schedules monthly talks by some of the area's most accomplished professionals and provides a great opportunity for curious adults from the community to learn new things and exchange ideas in a relaxed atmosphere.

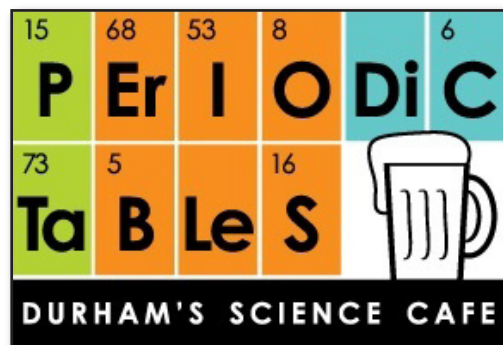
In his talk, [Wilcox](#), who is the head of the Reproductive Epidemiology Group at NIEHS, explained the structure of the human reproductive systems. He began the talk by polling the audience about their knowledge of reproductive biology and observed that a number of discoveries about human fertility emerged from epidemiology studies.

Wilcox discussed newer technologies such as intracellular sperm injection, where a single sperm is injected into an egg in the laboratory. He also pointed to some of the "downright weird" aspects of reproduction, such as ectopic pregnancies and human chimeras. A human chimera results when the developing eggs and DNA of fraternal twins merge to form one individual.

The audience's attention was riveted as Wilcox demonstrated how an egg transits from the ovary to the oviduct. Standing on a chair, he used his body to simulate the female uterus with his arms as oviducts and his fingers as fimbriae, a fringe of tissue surrounding the opening of the oviduct. To the delight of the audience and with a little help from two volunteers who held up the soccer balls that represented ovaries, he demonstrated how the oviduct "notices" the egg when it leaves the ovary and "scoops up the egg" into the oviduct.

Commenting afterwards about Wilcox's animated presentation, Brad Herring, director of Nanoscale Informal Science Education at the [Museum of Life and Science](#), said, "I've never seen so many people stand up to snap cell phone pics or so many camera flashes going off at a Science Café." He noted that the crowd's enthusiastic response to Wilcox was an "indication of how creative and funny and lively the talk was." Herring called Wilcox's presentation an example of the "engaging speakers" and "lively discussions" the museum strives to bring to the "lifelong learning" program.

A [slidecast](#) of the talk is posted on the group's Web site, and speaker nominations can be made at the top left hand side of the webpage. The presentation is also available on the slideshare.net [Web site](#).



In a marked departure from the usual lecture-slide format of science talks, Wilcox, center, hammed it up with the help of his mother, left, and a volunteer from the audience. The helpers held the ovaries during his demonstration. (Photo by Laura Hall)



Wilcox spoke to a full house that included Errol Zeiger, Ph.D., J.D., center, a retired NIEHS scientist and freelance science writer. Also on hand from NIEHS were John Schelp and Nick Staffa, Ph.D., as well as Wilcox's colleagues Dale Sandler, Ph.D., and Clare Weinberg, Ph.D. (Photo by Laura Hall)



An enthusiastic audience showed its appreciation with a round of applause. One attendee said it was "pretty cool" and another "thought he did a great job." Science Café regular John Nesser said he "just loved it." (Photo by Laura Hall)



Host Brad Herring introduced Wilcox and said afterwards, "Wilcox will be an example [for other speakers in the series] to look up to." (Photo by Laura Hall)

(Laura Hall is a biologist in the NIEHS Laboratory of Pharmacology currently on detail as a writer for the *Environmental Factor*.)

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